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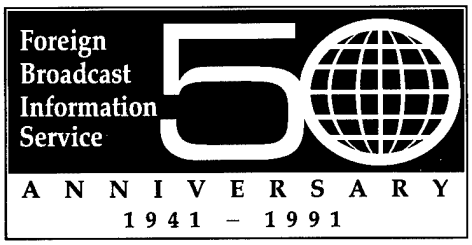
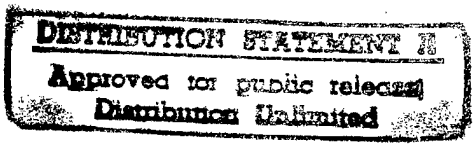


JPRS Report

Science & Technology

USSR: Life Sciences



Science & Technology
USSR: Life Sciences

JPRS-ULS-91-010 06 May 1991

CONTENTS

Biophysics

Biotechnology

Epidemiology

Genetics

Immunology

Industrial Medicine

Laser Bioeffects

Medicine

Microbiology

Molecular Biology

Nonionizing Radiation Effects

Pharmacology, Toxicology

Physiology

Public Health

Radiation Biology

Virology

Pharmacological Correction of Functional Condition of Army Air Force Flyers in Hot Climate With Asparkam

917C0083A Moscow VOYENNO-MEDITSINSKIY ZHURNAL in Russian No 7, Jul 90 pp 62-63

[Article by Col Med Serv A. A. Bochenkov, docent, and Maj Med Serv V. A. Chvyakin, candidate of medical sciences]

UDC 613.6:656.7]-07:615.2

[Text] Unfavorable conditions for flight personnel arise when crews fly modern aircraft in regions with a hot climate, where the temperature in the summer reaches 35°C or higher. The complex of climatic and geographical factors in such zones has a pronounced influence on the mechanisms of thermoregulation and the activity of systems such as the cardiovascular system (A. N. Azhayev, 1979). The functional condition of the flyer's body is impaired, and there are complaints of weakness, rapid fatigue, and poor efficiency. It takes longer to restore bodily functions that are altered during the flights.

Increasingly, a determination of the activity of succinate dehydrogenase (SDH) of the lymphocytes, a key enzyme of tissue respiration, has been used to characterize the functional condition of the body. For example, P. S. Pashchenko (1987) points out a significant correlation between the degree of decrease in activity of SDH and the cumulative flight time per shift. M. N. Kondrashova (1978) considers decreased SDH activity a characteristic symptom of incipient illness. A. S. Yanovskaya (1978) has demonstrated that delay in restoration of the activity of SDH until the next morning after physical exertion is an objective symptom of fatigue.

To improve the functional condition of the body of flyers, it is often recommended to employ vitamin preparations and vegetable and synthetic adaptogens—ginseng, eleuterococcus, leuzea, golden seal, and dibasol (N. M. Rudnyy et al., 1986). However, a pharmacological adjustment which produces a primary improvement in the cell metabolism, energy production, exchange of metabolites between organs, and adaptive synthesis is of greatest interest (Yu. G. Bobkov et al., 1984). Substances with such an action improve the trophics of nerve tissue, resulting in higher reserves of nervous regulation and better stability and functional quality of the nervous system. It is therefore no accident that drugs with primary metabolic type of action usually enhance both physical and mental performance at the same time, although to differing extent.

Out of the total number (91) of army air force flyers examined during flight duty in a hot climate, 10 were found to have low activity of lymphocyte SDH (1.05 + 0.01 standard units). That level was determined as per R. P. Nartsissov (1970). We also investigated the excretion in the urine of sodium, potassium, magnesium, and inorganic phosphorus by standard techniques with an adjustment to 100 mg of creatinine, which was determined in the same sample of urine, and we studied several psychophysiological factors. The drug Asparkam was used to adjust the functional condition of the flyer's body, in a dosage of one tablet three times per day for one month.

One week after administration of the drug, a reliable increase in activity of the lymphocyte SDH to 1.22 + 0.01 standard units was noted ($P < 0.01$). The activation of the lymphocyte SDH was accompanied by a change in the other indicators studied as well. For example, on day 14, there was a reliable ($P < 0.05$) increase in the excretion of sodium to 27.3 + 5.5 mmole from 14.3 + 2.3 and of potassium to 9.9 + 1.4 mmole from 5.6 + 1.0. Reliable changes in the dynamics of excretion of calcium were observed only toward the end of the monthlong course of pharmacological adjustment, when its level reached 7.11 + 0.92 mmole, as compared with 3.56 + 0.39 mmole before the start of the study ($P < 0.05$). By the end of the study, the excretion of inorganic phosphorus had increased to 3.8 + 0.7 mmole from 1.4 + 0.3 ($P < 0.05$). The dynamics of magnesium excretion was marked by inconstancy: by day 14 of the adjustment, its excretion had dropped to 2.5 + 1.2 mmole, whereas on day 28 it rose to 5.3 + 0.9 mmole, as compared with the original level of 4.2 + 1.3 mmole.

The influence of the drug Asparkam on the flyer's body consisted of a positive trend in metabolic shifts and improved functional condition of the body. That is evidenced by the dynamics of certain psychophysiological indicators. For example, by as early as day 14 of the study, the index of simple sensomotor reaction (in linear test) decreased to 11.3 + 0.6 cm from 16.7 + 0.8 cm ($P < 0.01$); on day 21 of the study, deviations in the stairs test amounted to 12.5 + 4.3 cm, as compared with 69.4 + 28.3 cm before taking the drug ($P < 0.05$). As early as on day 7, the speed of mental operations increased to 25.4 + 2.1 sec from 39.4 + 2.3 sec ($P < 0.05$). It should be noted that the increased speed of mental operations was attended by a corresponding decrease in the number of mistakes over a two-week period. For example, the number of mistakes on day 14 had decreased to 0.85 + 0.6 from 1.11 + 0.4.

Thus, use of the drug Asparkam in a therapeutic dose over the course of one month brings about an improvement in the functional condition of the flyer's body, as expressed by intensified tissue respiration (increased activity of lymphocyte SDH), a higher level of metabolic processes (increased excretion of sodium, potassium, magnesium, inorganic phosphorus), and better psychophysiological indicators (especially the indices of simple sensomotor reaction, the stairs test, and the speed of mental operations).

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Risk Factors and Prediction of Syncopic States in Flyers

917C0083B Moscow VOYENNO-MEDITSINSKIY ZHURNAL in Russian No 7, Jul 90 p 63

[Article by B. Kh. Semenov, candidate of medical sciences]

UDC 616.8-009.832-037

[Text] On the basis of many years of investigation and clinical observation by specialists of civil aviation, risk factors have been identified for the development of syncope in flyers—vascular and cardiac factors, the composition of the blood, autonomic tonus, factors which weaken the body, etc. In the context of those factors, the clinical data of 120 flight personnel were studied in four equal groups: those with repeated or onetime syncope, those showing vegetative-vascular dystonia without fainting, and healthy persons. On the basis of the findings of a correlation analysis, significant factors were discerned and given a rating on a point scale in accordance with the degree of closeness of the correlation curve. In the final variant, the risk factors for development of syncope and the point score corresponding to them were as follows: age 30 or under (6), tendency to low arterial pressure of 100/70 mm Hg or less (3), tendency to low blood hemoglobin content of 14.5 g/100 ml or less (3), tendency to low blood sugar level of less than or equal to the lower boundary of the normal level (3), hypotonia or venous dystonia of REG (5), presence of vegetative-vascular dystonia with prevalence of parasympathetic tonus (9), asthenization of the body caused by factors which weaken the functional condition, such as current or recent illnesses and intoxications, chronic fatigue and insomnia, conflict situations in daily life (7).

The risk factors were studied over a period of time in 100 persons. The catamnesis was tracked from one year to 20 years. The catamnestic data obtained made it possible to establish three degrees of risk and predisposition to syncope in flight personnel: if the number of risk factors (N) is two or fewer and the cumulative index (CI) of risk factors is 10 or fewer, the degree of risk is negligible and the prognosis favorable; if N is three and CI is 11 - 22, the degree of risk and the prognosis are indeterminate; if N is 4 - 5 and CI is 23 - 28, the degree of risk is high and the prognosis unfavorable.

We recommend that the risk factors identified and the technique worked out for evaluating the degree of predisposition to syncope be adopted in the medical flight examination as an auxiliary means of predicting syncope in flight personnel.

Survey of the Principal Results of Medical Research in the Flight Program of the Second Main Expedition Aboard the Mir Orbiting Complex

917C0096A Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 24 No 4, Jul-Aug 90 (manuscript submitted 23 Nov 88) pp 3-11

[Article by O. G. Gazenko, A. I. Grigoryev, S. A. Bugrov, A. D. Yegorov, V. V. Bogomolov, I. B. Kozlovskaya and I. K. Tarasov]

UDC 629.78:[612+613.693

[Text] The mission of the second main expedition aboard the Mir/Soyuz-TM/Kvant/Progress orbiting complex lasted from 6 February - 29 December 1987. Crew commander (KE-2) Yu. V. Romanenko was aloft for 326 days. Flight engineer (BI-2-1) A. I. Laveykin, who went up with him, worked for more than 175 days aboard the station, after which he was replaced by flight engineer (BI-2-2) A. P. Aleksandrov, who was aloft for 160 days. During the long-duration mission, the cosmonauts engaged in joint work with an international Soviet-Syrian visiting expedition, they received seven Progress cargo craft, they placed the Kvant special-purpose astrophysical module into operation and carried out scientific research with it, and they conducted three EVAs (11 April, 12 June and 16 June 1987), for a total EVA time of 8 hours 43 minutes. During the first (unplanned) EVA the crew carried out mechanical work associated with completing the docking of the Kvant module with the Mir orbiting station. During the second and third EVAs, it installed a solar panel that was being assembled.

The scientific flight program included continuing study of Earth resources and conduct of meteorological, astrophysical, geophysical, biomedical and other research.

Ongoing medical support to the flight, for the purpose of preserving and maintaining the health of the cosmonauts so that they could successfully complete the program, was achieved by creating adequate living conditions, by

maintaining medical monitoring (including thorough physical examination), by employing preventive resources against the adverse effects of the factors of prolonged flight, and by implementing measures for psychologically monitoring and supporting the crew.

The scientific medical program consisted primarily in continuing and expanding research on the phenomenology and mechanisms of change in the conditions of the principal body systems in the various stages of a long flight and after the flight was over.

General Description of Flight Conditions Aboard the Mir Station

We know from previous flight experience that creating favorable living conditions for the crew, providing it a balanced diet and a sensible work-rest schedule, and conducting a program of preventive measures are important for preserving the health and maintaining the performance efficiency of cosmonauts during and after a long flight.[1,4,8,12]

Living conditions were monitored during the flight and research was conducted in that area by a group of scientists under the supervision of I. G. Popov.

As a rule, microclimate parameters (temperature, humidity) and air composition (total pressure, oxygen and carbon dioxide partial pressure) in the station's crew living quarters were maintained during the entire flight within predetermined, hygienically favorable limits that were close to the parameters of the Earth's atmosphere. The subjective sensations of the cosmonauts generally agreed with data from objective monitoring of habitat parameters. The temperature and humidity conditions maintained most of the time (air temperature 22 - 25°C, relative humidity 37 - 66 percent) and the clothing worn by the cosmonauts, which had a thermal-insulation factor of around 1 CLO, provided them with sufficiently comfortable thermal conditions during minor physical exertion. That is confirmed to a certain degree by the relatively low water-consumption and the absence of intensive sweating and thirst.

The health-and-hygiene condition of the air of crew living quarters, which was assessed by gas-chromatography of air samples (samples were taken by the crew on sorbents and returned to Earth), was characterized by the presence in the air of traces of organic matter (identified as volatile human metabolites and products released by nonmetallic interior materials and onboard apparatus) of the following classes: aliphatic and aromatic hydrocarbons, alcohols, ketones, esters, aldehydes and hydrocarbon halides.

Most of the substances were acetone, acetaldehyde, ethanol and ethylacetate. The traces of organic matter generally had no appreciable effect on the condition of the air, which was assessed as being satisfactory.

The microbiological condition of the station's environment was characterized by the presence of isolated zones of accumulation and growth of Gram-negative bacteria (including conditionally pathogenic enterobacteria), sporogenic bacilli and mold fungi, represented chiefly by penicillins. Under certain conditions, those microorganisms not only may have medical significance, but may also cause biological destruction of polymers. During the flight, however, problems associated with the condition of the habitat never arose. To a certain degree, that was due to preflight measures involving limited observation, disinfection, and sanitizing, as well as to the use of a complex of hygienic equipment.

Personal hygiene measures included regular cleansing of the skin, the hair on the head, and the oral cavity, as well as compartment interior surfaces and eating utensils. The crew was provided with the following for those purposes: wipes for daily toilet; dry towels with which to wipe down the body and head after physical exercise and when changing underwear; oral hygiene resources, toothpaste and chewing gum; hair care resources; a set of toiletry articles; wipes with which to clean eating utensils; wipes for cleaning interior surfaces; washing agents in sealed packages.

The radiation conditions aboard the station were assessed as calm throughout the entire flight. The total dose received by the cosmonaut who was aloft for 11 months was 7,630 mrad, while for the other crewmembers it was 3,580 - 4,310 mrad over the course of 5 - 6 months of flight.

The food rations completely satisfied the energy and plastic needs of the cosmonauts' bodies, they were balanced in relation to all essential ingredients, and they kept the dietary status of crewmembers satisfactory. The average daily calorie intake was 3,100 - 3,200 kcal. Freeze-dried foods made up 65 percent of the rations.

Water was provided both from supplies transported and replenished from Earth and from water recycled from condensed atmospheric moisture during the flight itself. Water was used hot and cold. On the average, total water consumption was around 1.85 liters per day per cosmonaut (not counting food water and metabolic water). The maximum proportion of recycled water consumption was 69 percent.

The work-rest schedule of the main crew was planned on the basis of a 24-hour daily cycle, with two days off a week, which, as a rule, were on Saturday and Sunday. The nominal duration of the daily workday was 8 hours 30 minutes. Eight or nine hours were scheduled for sleep, and two hours were scheduled for physical exercise.

Over the course of the flight, there was some variation in the work load of the cosmonauts from week to week, because of particular features of different phases of the program. For example, in the initial period (the first two weeks of flight) the work load was planned at 50 percent below nominal in order to facilitate tolerance during the initial adaptation to weightlessness. The emergency docking with the Kvant module required the unplanned Vykhod [EVA] operation, during which the workday was

shifted and the duration of nighttime sleep was reduced to 4 - 5 hours. Later instances of overtime work were episodic, and they were adequately compensated for by additional free time and days off. During the final phase of the flight, the duration of the daily workday was somewhat reduced in order to allow for fuller implementation of preventive measures and preparation for landing. The responsible attitude of the cosmonauts toward planning of jobs and of the work-rest schedule played a large role in optimizing the schedule.

The complex of psychological support measures was directed at maintaining the psychological, emotional and working tone of the crew members, keeping their minds on their activity, and correcting for any detected changes in state resulting from the action of psychologically significant flight factors.[12]

The system of psychological support encompassed the following areas: furnishing the crew with information not related to their work (daily radio, news and music transmissions to the station); preparing and delivering with resupply craft equipment and programs for onboard recreation (musical and video programs, motion pictures, newspapers, literature); and diligent work with parties on the ground (families, representatives of flight control services, specialists, arts figures) to optimize contact with the crew.

The system of preventive measures implemented during the flight of the second main expedition was oriented on stabilizing the health and high efficency of the crew and preventing disturbances in the body's physiological systems during the lengthy flight, upon its termination, and in the postflight period.

Exercise on onboard physical-training equipment (an improved, combination treadmill equipped with a gravity-and-anchoring system, and an onboard bicycle ergometer), use of a set of expanders, and the wearing of weighted suits constituted the basis of the preventive measures over the course of the long-duration flight.[7,12,16]

Physical training on both machines was planned on the basis of a microcycle consisting of three training days and one rest day (a 3 + 1 cycle). The energy expended during the twice-a-day physical training over the cycle was 1,400-1,520 kcal.

The cosmonauts of the second main expedition, in accordance with the flight program, began their physical conditioning on the shipboard training equipment at the end of the first week of flight. By gradually increasing the volume and intensity of exertion, they were virtually at the planned level of the twice-a-day training in terms of the volume, intensity and structure of the exercises by as early as the end of the first month.

The recommended levels of daily locomotor exertion on the treadmill were 3,600 - 2,730 m at an average rate of around 125 m/min; on the bicycle ergometer, the levels were around 21,100 kgf/m at an average rate of around 800 kgf/m/min.[16]

The cosmonauts displayed a responsible attitude toward doing the physical exercises and following the recommendations of specialists. Based on the flight program and the condition of the cosmonaut, the physical exercises were tailored to the individual cosmonaut.

On the whole, the physical training of the cosmonauts was close to the recommendations in terms of the structure and organization of the exercises throughout the entire long-duration flight (Figure 1); in relation to some parameters, (rate, for example) the exercises surpassed the planned levels, which helped to maintain high cosmonaut efficiency during the flight and a favorable course of readaptation upon completion of the flight.

The program of preventive measures called for the wearing of special weighted suits (daily for not less than eight hours).

In the final phase of the long-duration flight (the last 2 - 3 weeks), a conditioning cycle involving application of negative pressure (-10 mm Hg, and subsequently down to -45 mm Hg) onto the lower body (NPLB) was conducted in order to stimulate neuroendocrine mechanisms regulating vascular tone, volume receptors, and liquid retention by the body and to prevent orthostatic instability during reentry and during the readaptation period. The NPLB conditioning schedule of the concluding phase of the 326-day flight included five preliminary and two final conditioning sessions in the days

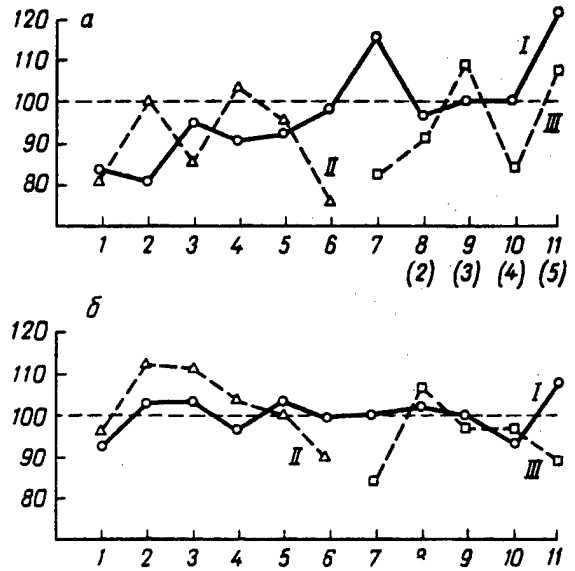

Figure 1. Volume (a) and average rate (b) of the locomotor exertion during the flight: *x*-axis, flight duration (in months); *y*-axis, magnitude of indicator (in percentage of recommended magnitude). I—326-day flight, II—173-day flight, III—160-day flight

preceding the end of the flight. The cosmonaut carried out NPLB conditioning under conditions close to those recommended; he reported that he felt good, and his arterial pressure and pulse rate exhibited extremely moderate fluctuations.

The complex of preventive measures carried out in the concluding phase of the long-duration flight also included the intake of water-salt additives on the last day of the flight and the wearing of a special preventive anti-G suit during the reentry phase and in the early postflight period. [3,6,7,12]

Results of Research During and After the Flight

General Description of Condition of Crew

All three crew members reported feeling good throughout the entire flight. The sensation of blood rushing to the head during the transition to weightlessness gradually abated, disappearing in approximately one week. One crew member developed vestibular-autonomic discomfort at the beginning of the flight. Episodically, after carrying out difficult jobs, the cosmonauts complained of fatigue, which appeared toward the end of the work day and left after a night's sleep. EVAs were followed by muscle fatigue and moderate pain in the muscles of the arms and the shoulder girdle, which disappeared over the course of one or two days.

The mental and emotional state of the cosmonauts (this research was conducted under the supervision of V. I. Myasnikov) was characterized by adequate adaptive changes. All crew members were highly motivated about carrying out the flight program. Group cohesiveness was high. Emotional responses were appropriate to the situations. Work activity was the leading component of overall mental state.

Sleep, as a rule, lasted 7 - 8 hours, and it corresponded to actual needs. In certain periods of flight (lasting 2 - 5 days), there were indications of difficulty in falling asleep, of light, interrupted sleep, and shifts of the sleep period into the "morning phase." Elements of emotional lability and changes in night sleep noted episodically in certain stages of the long-duration flight were eliminated primarily by adjusting the work-rest schedule and implementing psychological support measures. The efficiency of all cosmonauts remained at a sufficiently high level.

On the whole, the condition of the crew members was satisfactory at the touchdown site and in the immediate postflight period. After leaving the craft, the cosmonauts were able to walk on their own, although it was noted that they became tired more quickly, that their gait was shaky, and that they felt heavier. One of them noted an episode of vestibular-autonomic discomfort during independent walking in the first hours of flight. On the whole, the changes that developed in the functional state of the body were similar to reactions usually observed in cosmonauts following flights lasting several months, according to data from research by I. K. Tarasov et al. However, it is important to note that the degree of their expression in relation to many clinical and physiological indicators was lower than after flights of similar or shorter duration. The rate of recovery was relatively rapid, and the readaptation period proceeded favorably.

The medical problems that subsequently required a change in the crew composition of the second main expedition arose in BI-2-1 during the third month of flight, when disturbances in heart rhythm were detected in him during emotional and physical exertions. During an EVA (on 11 April 1987), a number of atrial extrasystoles with trigeminy were recorded in the cosmonaut when he underwent pronounced nervous and emotional stress. Later, soon after his EVA, pronounced tachycardia inappropriate to the exertion was observed, with a large number of supraventricular extrasystoles, when he was exercising on the treadmill under gradually increasing physical exertion.

Implementation of a number of medical measures, adjustment of the preventive program, and efficient organization of the work-rest schedule gradually normalized the heart rhythm during physical exertion. Thorough physical examinations and medical monitoring during the EVAs of 12 and 16 June 1987 revealed no disturbances of heart rhythm, and hemodynamic indicators did not reveal anything unfavorable at rest and in response to functional tests. But in late June, supraventricular extrasystoles appeared once again during a functional test involving physical exertion. The rhythm disturbances in the cosmonaut in response to physical exertion were not felt by the cosmonaut, and he reported feeling good in all stages; his efficiency remained rather high.

Analysis of the heart rhythm disturbances in BI-2-1 did not exclude the possibility that they would persist or grow worse during a long flight of up to 11 months, especially with the need for intensive daily physical training or the possibility of stressful situations. Such pronounced heart rhythm disturbances had never been encountered before in space flight. That necessitated exercising a certain degree of caution in terms of predicting the cosmonaut's state over such a long flight, and it ultimately resulted in the decision to replace the flight engineer when the next visiting crew reached the craft.

Postflight cardiological examination of BI-2-1 did not reveal any organic changes in the myocardium. Nor were disturbances in heart rate observed in response to physical exertion. From all appearances, the inflight heart rhythm disturbances may have been the consequence of a neuro-autonomic dysfunction taking the form of individual reaction of cardiac activity to the complex of flight factors. It should be noted that the nature of the cosmonaut's readaptation did not differ appreciably from that of the other cosmonauts.

Anthropometric Analysis

As we know, cosmonauts lose body weight in most cases. Weight loss in the 11-month flight varied from 0.6 to 2.1

kg. Change in body weight of the other two crew members was oppositely directed: it decreased by 0.6 - 3.4 kg for one of them, while for the other, who was underweight at the beginning of the flight, the indicator subsequently grew to where it exceeded the initial value by 2.4 kg.

Lower leg volume decreased steadily, volume loss was 5 - 18 percent in different phases of the flight, but by the end of the flight the loss did not exceed 12 percent.

Torso length (seated height) of all cosmonauts increased by 10 - 25 mm, with the increase occurring chiefly in the first month of flight.

The Motor Sphere

Research conducted in the postflight period by I. B. Koslovskaya et al. revealed changes in all components of the motor sphere of the crew members. Those changes fit completely within the framework of values noted earlier for long-duration flights, and they were characterized by a distinct dependence on the volume, form and intensity of physical exertion experienced during flight.

Changes in the speed and power properties of muscles of the lower leg and thigh and growth of electromyographic cost of a vertical posture were less pronounced for KE-2, who trained regularly twice a day, than for the crew member who trained only once a day on the treadmill for more than two months during his 160-day flight.

In the early readaptation period, changes in coordination and posture indicators (growth of the time to adjust the posture to perturbing effects, and growth of the amplitude of the electromyographic adjustment response) were greatest in the cosmonaut who (at the recommendations of the medical group) limited the length of his locomotor exertions.

In the postflight period, the smallest changes in the locomotive sphere were noted for KE-2, who was aloft the longest—326 days. Recovery of indicators characterizing the state of the motor system was relatively fast (around two months) for all three crew members, especially the commander.

Cardiovascular System

Bioelectric activity of the myocardium. The principal changes (according to data from 12 commonly accepted EKG leads) manifested themselves chiefly in the repolarization phase, and they were characterized by diffuse reduction of T-spikes (by 13 - 64 percent), predominantly in left thoracic leads; for one of the cosmonauts they were also observed in the standard and amplified leads on the limbs, which was concomitant in him with various T-spike deformations. On the basis of EKG analysis during tests involving metered physical exertion, those deformations were interpreted as functional deformations resulting from autonomic and metabolic changes.

Hemodynamics. Changes in the hemodynamics of resting cosmonauts fluctuated up and down, and in many ways they reflected the individual features of each of them.

The general patterns of those changes in all crew members during the flight manifested themselves as a tendency toward a decrease in minimum arterial pressure and growth in nominal values (calculated from phlebogram indicators) for pressure in the pulmonary artery (using A. S. Melentyev's method) and as inconstancy of filling of the jugular veins (the a/s index on the phlebogram), as well as a tendency for minute volume to decrease in two crew members and increase in one. Fluctuations in the principal hemodynamic indicators were close to preflight values in KE-2 during the longest (326-day) flight (Figure 2).

Polyrheographic analyses revealed general trends in the changes in a number of indicators: a reduction of the tone of cerebral vessels (mostly on the right side) and development of tonal asymmetry coupled with signs of difficulty in venous return, as was evidenced by the appearance of pronounced venous waves; reduction of the tone of upper limb vessels; reduction of pulse filling of vessels of the lower leg, coupled with an increase in their tone.

Besides the general patterns described above, each cosmonaut displayed individual features in hemodynamic response in flight. However, on the whole, circulatory

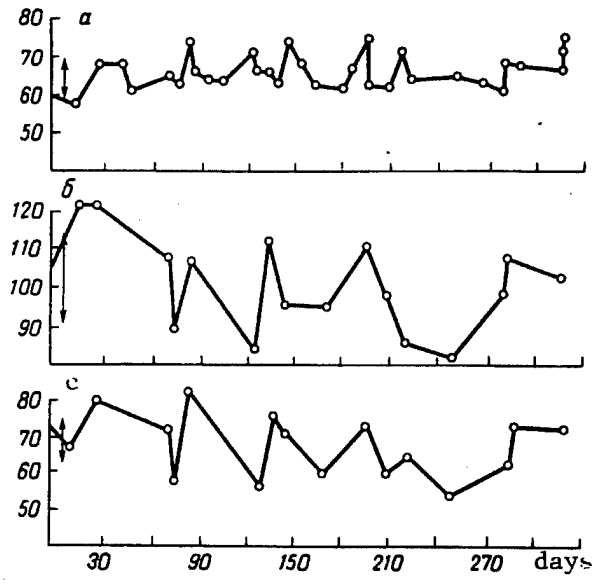

Figure 2. Changes in circulation indicators at rest in the cosmonaut during the 326-day flight: a—heart beats per minute, b—heart stroke volume (in ml), c—circulation minute volume (in liters/min). The arrow shows the indicator's fluctuation limits prior to the flight

system response to flight conditions may be assessed as adequate for all crew members.

A functional test involving application of NPLB during flight was accompanied by generally adequate responses of hemodynamic indicators, which did not differ appreciably from preflight values. NPLB has a normalizing effect on the tone of vessels in the head, as was observed for most of the cosmonauts. However, the tone of vessels in the head did not normalize in response to NPLB in one of the crew members, while in another the heart rate increased more abruptly than prior to the flight (to 94 - 101 beats per minute, as compared with not more than 85 beats per minute prior to the flight).

The research showed that the circulatory system can maintain high functional stability even during a 326-day flight—the longest flight to date.

The test involving gradually increasing physical exertion on a treadmill consisted of four graduations (from walking to a fast run) performed with the treadmill idling; the energy expenditure was about 100 kcal, and the total duration (including a final walk) was 11 min (Figure 3).

In two cosmonauts, the response of the heart rate to the test did not change in comparison with the preflight period; in the case of KE-2,it gradually declined, reflecting the training process.

However, the heart rate of BI-2-1 was 200 beats per minute by as early as the slow running stage at the end of the third month, and supraventricular extrasystoles appeared on the EKG (see above).

A two-step test with metered physical exertion on the bicycle ergometer elicited appropriate responses on the part of the circulatory system. Tolerance of the test by all cosmonauts was assessed as good or satisfactory in different phases of the flight. The heart rate and other hemodynamic indicators were closest to the preflight values in KE-2 in the 326-day flight.

Effective coronary blood flow (ECF) and the appropriateness of its change in response to one-step metered physical exertion during flight (750 kgf/m) were assessed by V. S. Bednenko, Ye. A. Milova et al. by means of ultrasonic Doppler cardiography in a specially developed procedure.[2] At the end of the first month and beginning of the second month of flight, the ECF response in the test with metered physical exertion was the same for one of the cosmonauts as it had been prior to the flight, whereas it decreased somewhat for the two other cosmonauts. When a test with metered physical exertion was conducted in the seventh month of flight (on only one cosmonaut), the ECF increment was noticeably smaller than prior to the flight. A similar direction of change in ECF in the metered physical exertion test was revealed in studies conducted on previous flights, particularly in the seventh and eighth month of a 237-day flight. That was evidence that change occurs in the mechanisms of regulation of coronary circulation under

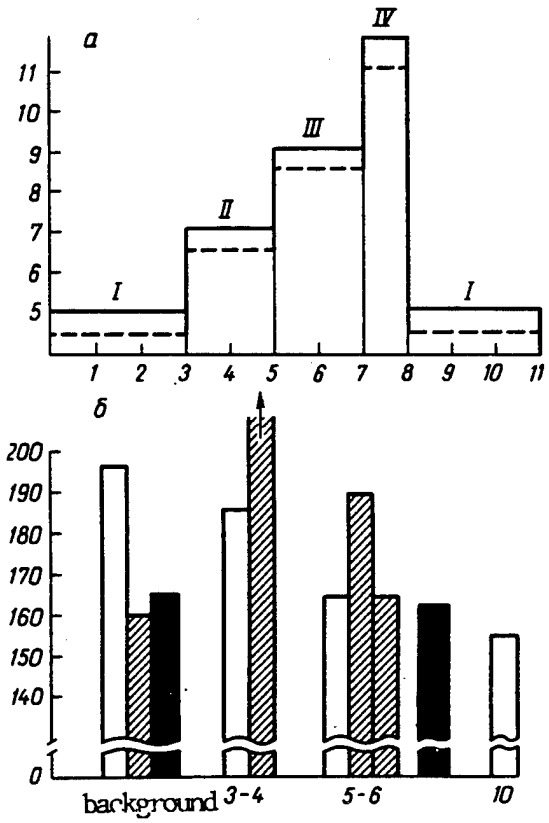

Figure 3. Diagram of graduated locomotor exertion (a) on a treadmill and the maximum heart rate (b) of the cosmonauts performing it. Solid and broken bold lines—stages of exertion (upper and lower limits). Upper graph: *x*-axis—time (in months); *y*-axis—exertion (km/hr); I—walking, II-IV—running. Lower graph: *x*-axis—flight duration (in months); *y*-axis—heart beats per minute; white columns—326-day flight, shaded columns—175-day flight, black columns—160-day flight

such conditions. However, a pronounced decrease in the ECF increment in a metered physical exertion test does not mean that that parameter is inadequate for the metabolic needs of the myocardium, since in the period of restitution following the metered physical exertion, no signs of an appreciable increase in the indicator were noted. In the opinion of V. S. Bednenko, one of the possible causes of this apparent contradiction lies in the hypothesized development of the phenomenon of dilation of reserve capillaries of the myocardium during flight and, associated with that increase, the perfusion of cardiac musculature by blood in a resting state, which creates a physiological reserve of oxygenated blood and thus reduces the "reaction" of the ECF index to metered physical exertion. The discovery of that phenomenon in animals after flights aboard biosatellites is a confirmation of the hypothesis.[15] Ultrasonic studies of the state of internal organs (liver, spleen, kidneys, lungs, prostate gland) were conducted by Bednenko et al. before and after the flight, and during the eighth month of flight

(liver, lungs) by means of Soviet-made Argument-A-1-OT apparatus (with the participation of Ye. P. Milova).

Growth of the anteroposterior dimension of the liver and filling of the lungs (more distinct in the lower and middle lobes) was detected during the flight.

An examination conducted during the first day after the flight on all three crew members revealed that the change in liver configuration remained, with growth of its linear dimensions; that lung filling has increased and undergone redistribution; and that the kidneys were enlarged. An increase in liver volume and spleen size and a reduction of the sagittal dimension of the prostate gland were observed in two cosmonauts. Those indicators tended to normalize by the seventh day.

The most probable cause of enlargement of a number of internal organs during weightlessness is redistribution of blood and its deposition in internal organs. In particular, deposition of blood in the liver, which is a "state indicator" of the right heart, may be viewed as an adaptive reaction preventing development of hypertension in the lesser circulatory system. The change in the state of the regulatory system directed at establishing and maintaining water-salt homeostasis in weightlessness may also play a certain role in kidney enlargement. We cannot at the moment exclude the possibility of the development of "stagnant" phenomena in renal capillaries, together with vasoconstriction of outgoing renal vessels and accumulation of liquid in interstitial spaces. This hypothesis is confirmed to a certain degree by the 20 - 28 percent weight increase invariably observed in the kidneys of animals (rats) after flights aboard the Kosmos series of biosatellites (605, 782 and 936), accompanied by a plethora of medullar vessels and the juxtaglomerular apparatus, as well as by activation of the renin-angiotensin system.[10]

Change and redistribution of lung filling may be promoted by the "damper" properties of the pulmonary vascular region, as well as by hypothesized activation of relieving reflexes in weightlessness.

Postflight Biochemical and Laboratory Analyses of Blood and Urine

Hormonal status. Research on the hormonal status of the body conducted under I. A. Popova revealed elevated activity of the hypothalamohypophyseal-adrenal and sympatho-adrenal systems, which manifested itself as an increase (1.5- to 3-fold) of blood cortisol level in all three cosmonauts during the first day after the flight and persistent elevated levels of epinephrine and norepinephrine in the blood for one week (Figure 4), with elevated excretion in the urine of free and bound forms of epinephrine, norepinephrine, dopamine and their methylated derivatives. The body's endocrine responses, which result in stress development, had certain individual features manifested in particular as an increase in

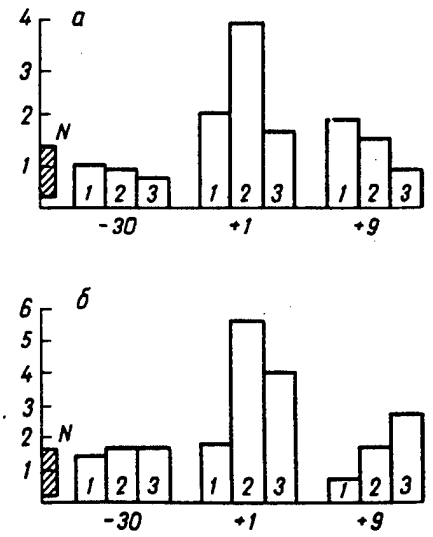

Figure 4. Indicators of sympatho-adrenal activity of cosmonauts before and after the flight: a—epinephrine concentration (in g/liter), b—norepinephrine concentration (g/liter). N—normal values, 1—326-day flight, 2—175-day flight, 3—160-day flight. Analysis times: -30 represents the point 30 days prior to the flight; +1 and +9 represent day 1 and day 9 of readaptation

the level of ACTH in the blood in only one cosmonaut and as a decrease in that hormone's concentration in the two other cosmonauts.

As was demonstrated after other flights as well, development of a stress response is typical of the initial period of readaptation (regardless of flight duration) and, to a large degree, is the product of the dynamic factors of the final flight phase and of the return to Earth.[4,8,12] The degree of expression of the manifestations of readaptation stress may depend, to a certain extent, on flight duration, which, as was established earlier, is characterized not so much by changes in the indicators of functional activity as by the responses of actuating organs and systems.

On the first day after touchdown, blood levels of growth hormone were lower in all the crew members, while two cosmonauts exhibited an increase in the concentration of prolactin, which inhibits gonadotropic hormones. It is probably because of that that all crew members showed an increase in the concentration of follicle-stimulating hormone in blood, while one crew member showed a drop in hypophyseal luteinizing hormone.

Water-salt metabolism. Daily diuresis was somewhat lower during the first 3 - 5 days after the flight against the backdrop of elevated water consumption; that is a typical response to long flights.[5,6] Excretion of the principal electrolytes (sodium, potassium, chlorine) in the urine was lower, and activation of the renin-aldosterone system, which promotes retention of liquids and salts by the body, was observed.

The potassium levels in the blood were lower in all three cosmonauts, but to a greater extent and for a longer time (9 days) in the cosmonaut who had been aloft for 326 days; his blood aldosterone level remained high for a longer time as well.

The levels of total ionized calcium in blood serum on the day of touchdown increased, as did the excretion of that ion in the urine for several days after the flight, which was also observed after other long expeditions.[6]

A decrease in the concentration of calcitonin in the blood, which reduces the calcium level in blood plasma, was observed to persist after 326 days of flight for nine days in the presence of a normal or slightly elevated level of parathyroid hormone.

Thus, as in previous long-duration flights, changes in the water-salt metabolism showed up as dehydration of the body, loss of calcium and potassium ions, and responses of hormonal regulatory systems directed at replenishing the volume and ionic composition of the body's liquid media. Loss of potassium, but not calcium, may be associated to a larger extent with the amount of time spent in weightlessness.

State of bone tissue. According to single-photon absorptiometry, only the cosmonaut who was aloft for 326 days exhibited a 5.6 percent decrease in mineral density of the diaphysis of the tibia, which corresponds to existing ideas about the responses of compact bone structures to diminished functioning.

It should be noted that the degree of expression of those changes was not any greater than that observed in some cosmonauts who had been aloft for shorter durations. Comparing those data with the results of model research[9] permits the hypothesis that the degree of demineralization of the tibia in flight depends, to a large extent, on the volume and schedule of physical conditioning.[14]

Energy metabolism. I. A. Popova et al. determined the levels of energy substrates and intermediate metabolic products and the activity of certain enzymes in blood serum in order to identify the features of energy supply to the body after flight.

In contrast to previous flights, energy production in all crew members after the second main expedition (EO-2) mission (regardless of duration aloft) was provided chiefly by carbohydrate substrates, with a substantial elevation of the proportion of glycolytic and anaerobic transformation. That was reflected in a moderate increase in blood glucose concentration (6 - 8 millimoles/liter) and in levels of lactic and pyruvic acids—metabolites of carbohydrate metabolism which accumulate in blood during intensive transformation of glucose during glycolysis and with reduced utilization of those metabolites by tissue. A higher pyruvate concentration was noted in the blood of KE-2, who was aloft the longest. The hormonal reaction in response to hyperglycemia manifested itself in one of the three cosmonauts by a decrease in the blood insulin level, and in the two others by an increase.

After the flight, research on the dynamics of the substrates of fat metabolism revealed a decline in the level of blood triglycerides (the most important of the forms of energy accumulation available to the body) in two cosmonauts and its increase in one. The concentration of free fatty acids in the blood (in contrast to the results of most prior studies) was reduced in two cosmonauts.

Analysis of two enzymes of the Krebs cycle in blood revealed a decrease in the activity of malate dehydrogenase—depending on flight duration—and of isocitrate dehydrogenase. A previously obtained relationship between degree of activity and flight duration was not confirmed for the latter enzyme.

The hypothesis exists that the mechanism by which energetically less advantageous energy consumption pathways (carbohydrate substrates coupled with an elevated proportion of glycolytic and anaerobic transformations) are activated and/or predominantly utilized should be sought in changes in the structure of the interrelationships between the principal factors, mainly of hormonal nature, that control accumulation and metabolism of energy substrates entering the body.[11]

Clinical and laboratory blood analyses carried out by V. I. Legenkov et al. revealed that the reticulocyte count in the peripheral blood of all the cosmonauts of the main crew was lower by an average of 27 percent in the first hours after touchdown. Later (by days 9 - 11 of readaptation), the reticulocyte count gradually increased. As in previous long-duration space flights, hematological indicators in all cosmonauts were observed to drop during days 3 - 11 of readaptation: hemoglobin levels dropped by 4 - 14 percent, the erythrocyte count decreased by 13 - 30 percent, and hematocrit decreased somewhat as well (by 2 - 5 percent).

Erythrocyte metabolism. According to research carried out under A. S. Ushakov, a decrease in the rate of glycolysis and a certain decline in the concentration of ATP in erythrocytes were detected in the first days after the flight. Investigation of the redox system revealed a substantial decrease in the concentration of reduced forms of glutathione, which may be associated both with reduced synthesis and with growth of the activity of the oxidative form, which elicits an increase in the intensity of oxidative processes in the cell. The latter circumstance may be a precondition for activation of free-radical processes and oxidative breakdown of membranes.

The changes found in metabolic status of the cell correlated with changes in membranes that were characterized by an increase in the level of free cholesterol and its esters, reduction of the concentration of phospholipids, and change in the ratio of phospholipid fractions in relation to each other and cholesterol. It was established that in the early period of readaptation after a long space

flight, destabilization of membrane components leads to substantial metabolic changes, to lower deformability of cells, and to growth of membrane rigidity.

The changes found in the indicators of erythrocyte metabolism were also noted previously after long space flights. They did not progress when the flight duration was increased to 326 days.

State of the immune system. The state of the T- and B-immune systems and humoral mediators, allergological status, and auto-immune changes were studied after the flight (I. V. Konstantinova et al.).

As with other long flights, the viral resistance of the body was found to be lower in all cosmonauts, evidenced by a decrease in functional activity of natural killers. A change in the capacity of those cells to attach to target cells, which include the cells of virus-infected tissues, was also found. That is why the decrease in viral resistance may have been associated with inhibition of expression of the cellular receptor apparatus.

Investigation of humoral mediators that have a regulatory influence on the immune system revealed reduced lymphocyte synthesis of interleukin-2 in two cosmonauts and reduced endogenous α-interferon in one. Synthesis of γ-interferon did not change appreciably. Most of the changes that were found one day after touchdown, and then one week and 14 days later, returned to normal. Successful performance of a complex of preventive measures during the flight by the members of the crew was probably the reason for the rather rapid recovery of immune resistance.

Signs of sensitization to formaldehyde—one of the constantly encountered components of microimpurities in the sealed inhabited spaces—were found in two cosmonauts. That reaction was also noted among certain cosmonauts after previous long-duration flights.

Microbiological analyses. The microbiological examination that A. N. Viktorov et al. conducted of the crew members before, during and after the flight did not reveal growth of dysbiotic changes. Growth of the concentration of groups of microorganisms significant to diagnosis of dysbacteriosis (staphylococcus, conditionally pathogenic enterobacteria etc.) was not observed in any of the investigated biotopes (upper respiratory tract, digestive tract, skin surface). Intestinal bifidoflora maintained a certain stability. The decrease found in the concentration of lactoflora was less pronounced than in previous long-duration flights. The results indicate that the complex of epidemic-control measures and sanitation methods used by the crew members—including use of a eubiotic-bifidum-bacterin preparation and personal hygiene resources having a preventive action—were effective.

Conclusion

The most important result of the medical research carried out during the flight of the second main expedition aboard the Mir station is the fact that Yu. V. Romanenko's flight of 326 days (three months longer than the longest previous flight) and the diligent activity he carried out during that time were not accompanied by the development of functional changes that were fundamentally different from those observed on other flights. He maintained high functional stability and sufficiently high efficiency throughout the entire flight; that was because of the sensible determination of the work-rest schedule and of all vital activities aboard the station by the crew and ground services, and regularly performed preventive measures of the proper amount, above all, regular physical exercise. Those circumstances also had a positive effect on the cosmonaut's condition after the flight.

In the postflight period, not a single cosmonaut exhibited any functional changes (or their progression), on the part of the main body systems, that were fundamentally different from those observed in other long-duration flights.

The readaptation period proceeded extremely favorably. On the whole, the health of Yu. V. Romanenko after the flight corresponded to preflight predictions, and the reactions that did occur (a moderately pronounced decrease in orthostatic resistance to physical and orthostatic loads, changes on the part of the motor sphere and some biochemical blood indicators, etc.) corresponded to those usually observed in cosmonauts after long flights. Moreover, his postflight status was even better than those observed after shorter flights in terms of a number of indicators characterizing the body's main systems.

All changes found during and after the flight corresponded to the factors to which the cosmonauts were exposed, and apparently they were adaptive in nature, they were reversible, they did not have an effect on performance during the flight, and they gradually returned to normal during readaptation.

It should be noted that throughout the entire flight, all crew members were systematic, exceptionally precise and creative, and individual in their approach to carrying out all recommendations on the use of means to prevent the unfavorable effects of weightlessness.

Thus, as shown by the experience of trips into space that last many months, although development of physiological changes of one degree of expression or another is unavoidable on long-duration flights, the effect of prolonged weightlessness may be successfully countered by a complex of preventive measures.

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State-of-the-Art Automated Evaluation of Functional State of the Body in the Space Program and Preventive Medicine

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[Article by B. A. Adamovich, R. M. Bayevskiy, A. P. Berseneva and I. I. Funtova]

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[Text] Development of methods and means for evaluating the functional capacities of the body during space flight is one of the leading problems of space medicine. As specially selected and trained healthy individuals, cosmonauts have a high resistance to various adverse environmental factors, and they have a large reserve of functional resources. However, long-term presence in weightlessness for a period of several months requires constant exertion of adaptive mechanisms in order to maintain the balance between the human body and the environment. Medical monitoring of cosmonauts is geared to evaluating and predicting the functional capacities of both the body as a whole and its individual systems; in particular, much attention is devoted to the circulatory system.

An essential feature of the medical monitoring of space flight crew members is the need for rapid processing and analysis of information for the prupose of the rapid acquisition of the data needed for making decisions in the complex, changing conditions of flight. That is what is behind the development of automated information analysis systems. One of the important objectives is the standardization and automation of the evaluation of the results of medical monitoring, which considerably raises the objectivity of medical conclusions concerning the body's functional capacities. The significance of this aspect of the automation of medical monitoring stems from the fact that health criteria are developed to a lesser degree than are disease criteria, and identification of the functional states of a healthy person cannot fully rely on the experience of clinical medicine. At the same time, even minor changes in the functional capacities of the body must be taken into account in the medical monitoring of cosmonauts, because their evaluation is essential to the prediction of unfavorable changes and to their prevention. That is why one of the most important requirements imposed on automated systems for evaluating the functional capacities of the body in space medicine is that, in addition to being capable of primary processing of medical information and its analysis, they must be able to rapidly organize the raw data used in making integral evaluations. Such evaluations must be the result of objective "weighing" of individual indicators, parameters and qualities of the human body, and ultimately they must characterize the health of the individual and his functional capacities.

In their 1967 book "Space Cardiology," V. V Parin et al.[23] proposed viewing the cardiovascular system as an indicator of the adaptational responses of the whole body. Changes in the heart and vessels play the leading role in the conditions of space flight, and especially in its initial period. The reason for that lies primarily in the fact that the shift of body fluids to the upper portion of the body as a result of the absence of gravity leads to a change in the hemodynamic balance and to overfilling of the pulmonary vascular channel. As we know, one of the leading means of preventing the adverse effects of weightlessness on long flights is regular physical exertion that promotes, in particular, relief of the lesser circulation and maintenance of the functional capacities of the heart at a level close to that observed on Earth.[25] At the same time, regular performance of physical exertion requires certain energy outlays and a corresponding mobilization of functional reserves. The body's adaptation to space flight conditions consists of a number of stages: an acute stage, a stage of relatively stable adaptation, and a stage of stable adaptation.[14] Mobilization of protective-adaptive mechanisms enable the maintenance of a hemodynamic balance close to that on Earth. However, it is attained at a higher price because mobilization of functional reserves requires high exertion of regulatory mechanisms.

Thus, the functional capacities of the body, and particularly of the cardiovascular system, depend not only on functional level—that is, on the values of the principal vitally important parameters—but also on the "price" that the body must pay for that. The higher the exertion of regulatory mechanisms responsible for mobilizing the needed functional reserves, the higher the "price" of adaptation. Consequently, the functional capacities of the body may be assessed by analyzing indicators characterizing the functional level of individual systems, their functional reserve and the degree of exertion of regulatory mechanisms.[4] The transition from health to disease, from the norm to pathology, is a process involving the gradual increase of the "price" of the body's adaptation to environmental conditions. Prolonged exertion and overexertion of regulatory systems leads to their exhaustion. Disturbance of function-regulating processes elicits, first, functional changes in the body and then morphological changes—that is, development of disease. Consequently, health represents a certain level of functional capacities of the body, it is its particular capacity for adapting to environmental conditions (its adaptive potential), it is maintenance of homeostasis in the face of inadequate environmental factors.

A scale consisting of four gradations of functional capacity has been developed to evaluate adaptational potential (level of health): (1) high or adequate functional capacities of the body, satisfactory adaptation to environmental conditions; (2) a state of exertion of adaptive mechanisms that ensure sufficient functional capacities through the mobilization of additional functional reserves; (3) lowered functional capacities of the body, unsatisfactory adaptation to environmental conditions; (4) low or minimal functional capacities of the body, failure of adaptation.[4]

The scale of the change in the functional capacities of the body reflects a gradual decline of adaptational potential and an associated transition from complete health to borderline states between the norm and pathology, and then to disease, which is nothing more than the "floor" of the protective mechanism. The zone of borderline states is of the greatest interest in research involving healthy individuals. It is advisable within that zone to make a distinction between states that are closer to the norm (so-called prenosological states[3]) and states closer to disease (so-called premorbid states[4]). A rather vast body of literature exists in regard to premorbid states. The problem of pre-disease has been tackled by many prominent clinical researchers.[2,12] But as far as prenosological states are concerned, they have only quite recently become a topic of research, with space medicine occupying the leading place in that regard.

A state of exertion of adaptive mechanisms is typical of space flight. It is usually observed in the period of acute adaptation and during the performance of the most critical operations. Such a state may develop in the direction of normalization (the "price of adaptation" falls) or in the direction of overexertion and exhaustion of regulatory mechanisms (the "price of adaptation" rises). A method of predicting the functional state of crew members making it possible to determine whether there is a favorable or an unfavorable trend in the changes in the functional capacities of the body has been developed on the basis of that approach.[5] The approach was developed further on the basis of the results of its testing on Earth on large groups of the population during mass preventive examinations.

Mass cardiological examination programs geared to detecting the principal cardiovascular diseases and the factors causing them are now widely used in our country and throughout the entire world. In addition to traditional epidemiological research in which the primary focus is on determining the risk factors of disease development,[19] a large complex of examinations that use the approaches described above have been conducted to evaluate the functional capacities of the circulatory system.[17,22] Those examinations were conducted on organization-attached groups of workers at industrial and agricultural enterprises, and they included healthy people, people in the borderline zone between the norm and pathology, and people with compensated forms of disease.

The research results showed that the functional state of essentially healthy people largely depends on the body's capacity to adapt to the environment and on the functional reserves of the main vitally important organs and systems. In turn, the functional reserves determine the degree of exertion of regulatory mechanisms that is needed to achieve a balance between the body and its

environment. Those studies were the basis for developing a new scientific area—prenosological diagnosis, i.e., identification of states of the human body on the borderline between the norm and pathology.[17] It should be noted that space medicine has been a major contributor to the development of prenosological diagnosis. One of the new "proving grounds" for testing its approaches was a mass screening system.

A serious, diligent effort was initiated in 1981 to create a new type of mass health screening system that would be based on evaluation of health and would use that evaluation to effect early diagnosis and prognosis of disease. Thanks to those efforts, the ideas and methods of space medicine achieved practical embodiment in the form of medical-equipment, instrument, and software systems for mass preventive examinations of the population. One of the first such systems was the Avtosan-82 mobile automated laboratory, designed for quick evaluation of health and remote medical examination of the population. The Avtosan-82 laboratory was created jointly by specialists in space and preventive medicine, and it was something of a ground-based analog of the medical monitoring system used on the cosmonauts. All of the equipment is housed in a LAZ bus (Figure 1). Figure 2 consists of block diagrams of the system for medical monitoring of the crew of the Salyut-6 orbiting station and of the Avtosan-82 medical equipment system. By and large, the structure of the systems is identical. The Avtosan-82 laboratory uses the onboard Aelita instrument system—a polyfunctional polygraph. The Avtosan-82 laboratory was on display at the All-Union Exhibition of the Achievements of the USSR National Economy, and its specifications have been published.[1]

Inasmuch as Avtosan-82 is the first medical-equipment system created by the linkup of space and ground-based medicine for mass preventive examinations of the population, we believe it would be suitable to examine its structure and function in greater detail. The cycle of analyses conducted by the laboratory consists of three stages. Anthropometric measurements (height, weight, dynamometry) are taken and lung vital capacity is determined in the first stage; cardiological analyses, at rest and during functional tests, are conducted in the second stage; six-lead EKGs and ballistocardiograms and seismocardiograms are recorded, arterial pressure is determined, and cardiac rhythm is subjected to mathematical analysis. Functional tests (active orthostatic test and 20 squats) are conducted together with measurement of pulse rate and arterial pressure. The third and final stage of examination is an autointerview, carried out in a dialog with the computer display. After the autointerview, the computer prints out a "Health Evaluation Chart" bearing the basic results of the measurements, an evaluation of functional state on a four-point scale, a list of individual risk factors, and recommendations on further examination by specialists of a particular profile.

The Avtosan-82 laboratory is designed to examine 10 - 12 persons per hour. It is serviced by four personnel—a physician, two nurses and a computer operator. A questionnaire method of information collection was used in the first two stages: measurements were entered on a registration card, which the operator used to enter data into the computer prior to the autointerview. The total examination time did not exceed 15 - 20 minutes. The laboratory accommodated three patients simultaneously. One of the unique technical concepts is a small bed for cardiological analysis with built-in electrodes and sensors, making it possible to quickly record EKGs and other cardiological signals without requiring the patient to undress.

The rapid health evaluation divides patients into four groups, based on different levels of adaptational potential. Persons with unsatisfactory adaptation to environmental conditions and with failure of adaptation as a result of suspected cardiovascular pathology can undergo a thorough cardiological examination. To do that, the Avtosan-82 laboratory is capable of recording an additional, 12-lead EKG, a rheogram, a sphygmogram, and a kinetocardiogram by means of the Aelita instrument. A system for remote recording of EKGs that uses a two-way teletype communication between the mobile laboratory and a consultative-prognostic center represents an important resource for thorough cardiological examinations. A remote examination could be carried out with either standard telephone channels or satellite communications.

The Avtosan-82 laboratory is the prototype of a number of automated systems developed in 1983 - 1987 for mass examination of the population. The Kardiosan mobile laboratory[20] and the Potok automated multilevel hierarchical system[21] have been created for preventive cardiology. Automated systems based on microcomputers[1] and based on YeS computers that enable the formation of data banks[12] have been developed for mass health screening .

One of the most important results of the interaction between space and ground-based medicine is the creation of a fundamentally new methodology of mass preventive examinations of the population that is geared to evaluating health rather than identifying disease. This also makes it possible to approach the organization of mass health screening of the population in a new way, to raise the effectiveness of preventive measures, and to effect monitoring of changes in the health of healthy people. The creation of automated systems of varying complexity and various purpose that are outfitted with the appropriate equipment and are based on standardized principles of health evaluation may be tailored to meet the objectives of medical practice. All such systems may be identified under the common term of "prognostic" systems, inasmuch as evaluation of the body's functional capacities, in characterizing the degree of adaptation to environmental conditions, also reflects the probability of transition to premorbid states or to adaptation failure. Repeat examinations can be used to

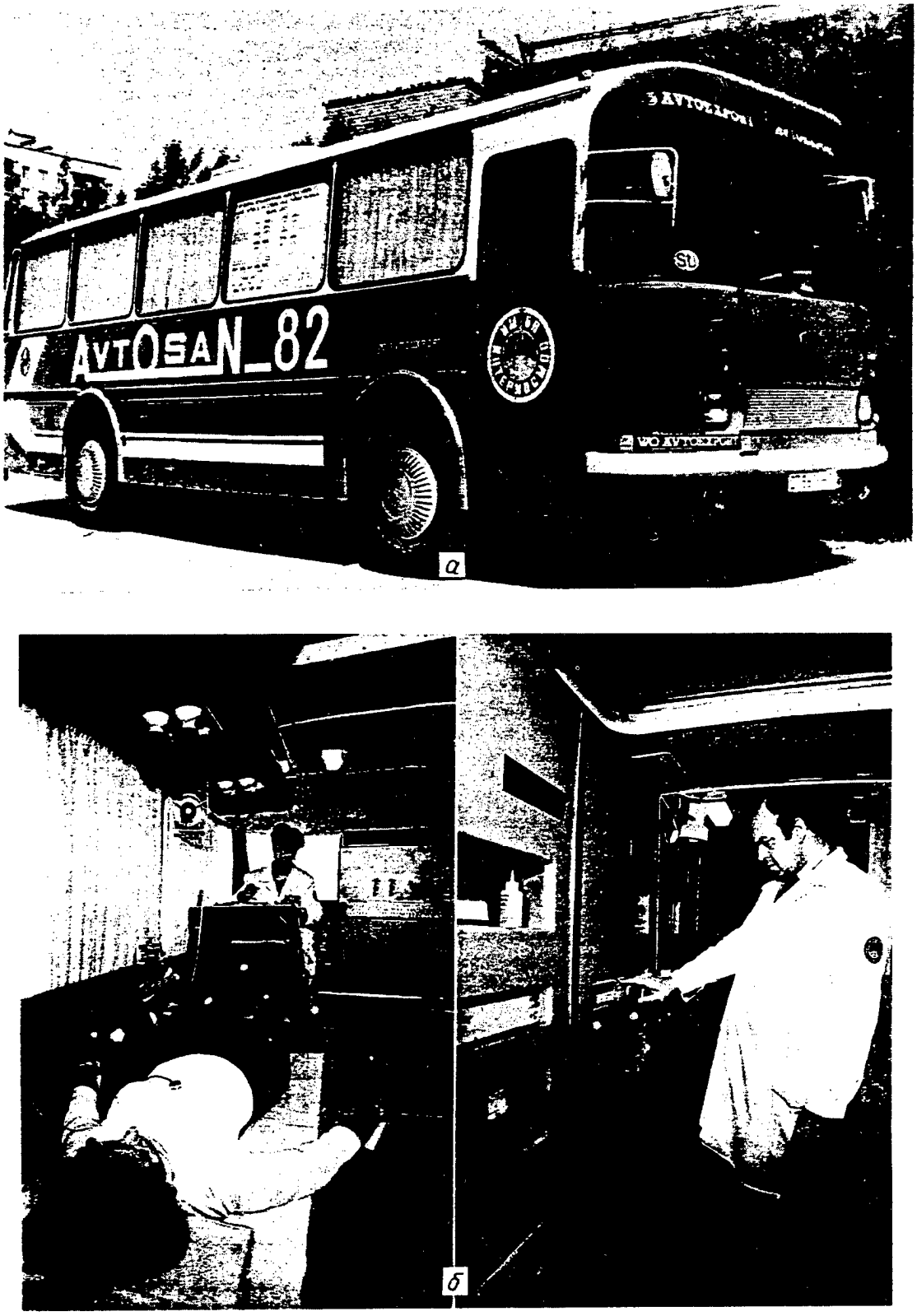

Figure 1. Exterior view of the Avtosan-82 mobile automated laboratory (a) and one of the examination stageing points in it (b)

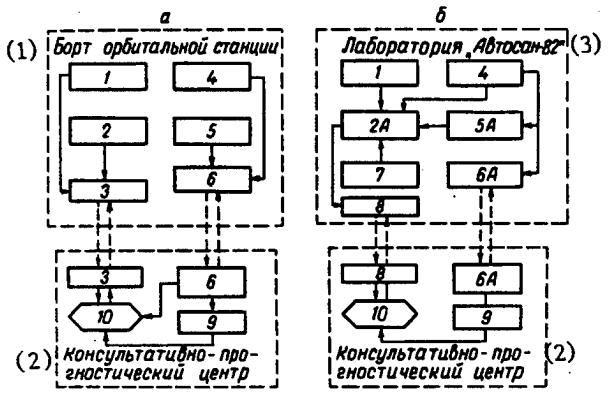

Figure 2. Structure of the medical monitoring system of the Salyut-6 orbiting station (a) and of the Avtosan-82 mobile automated laboratory (b): 1—anthropometric measurement system, 2—questionnaire system (dialog mode), 2A—autointerviewer (automated questionnaire), 3—radio intercom system, 4—Aelita polygraph, 5—on-line medical monitoring apparatus, 5A—automatic cardiac rhythm analyzer, 6—radiotelemetry system, 6A—system for transmitting EKGs by telephone, 7—automatic arterial pressure measuring unit, 8—teletype, 9—computer complex (YeS-1033 computer), 10—group of consulting specialists

Key: 1. Orbiting station—2. Consultative-prognostic center—3. Avtosan-82 laboratory

provide reliable data on trends in the change of functional state toward normalization or further disadaptation. We will examine below three types of automated prognostic systems developed for the objectives of preventive medicine.

The Kontrol system is intended for monitoring changes in the functional capacities of the circulatory system on the basis of a minimum set of signs. The system is designed for wide use in polyclinics, medical-health stations, preventoriums, and sanatoriums and in industrial medicine and labor physiology—in all cases where it is impossible or inadvisable to use expensive apparatus and where it is desirable to limit examinations to the traditional measurements of pulse rate, arterial pressure, height and weight. Analysis of the results of mass prognostic examinations of large contingents of the population have shown that those indicators vary considerably among people with circulatory systems that have different functional capacities.

An integral indicator—the index of functional changes (IFC)—was developed to enable monitoring of unfavorable changes in functional state. It is calculated by the formula

$$IFC = 0.011\ PR + 0.014\ SAP + 0.008\ DAP + 0.014\ A + 0.009\ W - 0.009\ H - 0.27,$$

where PR is pulse rate in beats per minute; SAP and DAP are, respectively, systolic and diastolic arterial pressure (in mm Hg); W is body weight (in kg), H is height (in cm), and A is age (in years). IFC assumes range from 1.00 - 4.00. The arbitrary boundaries for the ranges of IFC values that delineate various health groups are as follows: (1) for satisfactory adaptation, 2.59 or under; (2) for exertion of adaption mechanisms, 2.60 - 3.09; (3) for unsatisfactory adaptation, 3.10 - 3.49; (4) for failure of adaptation, 3.50 or over. However, the Kontrol system is used most effectively for observation of changes in health—for example, before and after a stay in a sanatorium or preventorium, before and after a course of exercises in a health group, and so on. Microcomputer programs have been written that make it possible to automatically calculate the IFC, compare the indicator's values after repeat examination, and determine the effectiveness of preventive measures to reduce probable morbidity.[7,8,10]

The Vita system is intended for use at the pre-physician stage of preventive examinations, including in mass health screening. Of the 439 criteria that make up the input information, 309 go on a questionnaire card and are collected in an autointerview conducted via computer display or in an interview of the patient in which the data are entered on a special form. A total of 130 criteria represent the results of objective examinations. An algorithm for analyzing all of the information collected enables a number of conclusions that are entered on the "Health Evaluation Chart". They include the following:

1. An evaluation of the functional state (FS) of the circulatory system, which is effected with a regression equation of the following form:

$$FS = 0.008\ PR + 0.008\ SAP + 0.006\ DAP + 0.18\ EKG + 0.56\ BKG + 0.001\ IE + 0.02\ W + 0.002\ H - 0.78,$$

where EKG and BKG are the degree of change of the EKG and the ballistocardiogram, respectively; IE is the index of exertion of regulatory systems as determined from mathematical analysis of cardiac rhythm[3]; and PR, SAP, DAP, W and H are defined as in the formula for determining the IFC.

It should be noted that this formula for determining FS was obtained by step-by-step regression analysis of the results of 2,000 examinations that were first evaluated by experts. The coefficient of correlation between the calculated evaluations and the expert evaluations is 0.86. The corresponding correlation coefficient for the IFC is 0.72.

2. Determination of the list of risk factors and their intensity by analyzing responses to questions concerning lifestyle and harmful habits and by analyzing objective data.

3. Determination of the probable pathology profile on the basis of data from objective examinations and the questionnaire.

4. Determination of the treatment group and the issuance of recommendations. Each subject is placed into one of three treatment groups as a result of analysis of data on patient functional state, risk factors and the probability profile of pathology: healthy, essentially healthy, or ill. Individuals in the third group have either subcompensated or decompensated forms of disease. Individuals with compensated forms of pathology are categorized as essentially healthy.

The Vita automated system is based on an SM-1420 minicomputer. Data is collected by two methods: (1) the questionnaire method of data collection can be introduced into virtually any polyclinic or medical-health unit, since it is based on the use of existing staffing subdivisions—the pre-physician examination office, the preventive department, the office of functional diagnosis, and the clinical laboratory. A standard form filled in with the results of the examinations made in those polyclinic subdivisions is forwarded to a computer center, which processes the data, sets up a database, and issues the "Health Evaluation Chart", which is sent to the polyclinic; (2) automated data collection involves the use of a system of electronic instruments linked to microprocessors or microcomputers, and the creation of automated workstations.

It should be noted that the Vita software system is a direct development of the work done with the Avtosan-82 mobile automated laboratory, and it takes into account the present state of the problem of mass preventive examinations of the population. A mass examination program approved by the CEMA Permanent Commission on Public Health was used to design the system.[15]

The Ritm system is intended for thorough evaluation of the functional health of essentially healthy people, for determination of the functional reserve of the circulatory system, and for observation of changes in health in response to unfavorable environmental factors. The system's principle of operation is based on a determination of the body's "price of adaptation" to various metered exertions. Physical, orthostatic, and mental stress were selected as such exertions in the first stage. The heart's sinus node or, more accurately, a changing series of values of cardiac interval duration is the indicator of the adaptive response to those exertions. Mathematical statistical analysis of a changing series of cardiac intervals makes it possible to thoroughly study its variability, which depends on autonomic balance (the ratio of the tone of the sympathetic and parasympathetic sectors of the autonomic nervous system), the state of subcortical nerve centers (vasomotor, thermoregulatory, centers controlling metabolism, etc.), and the state of the cerebral cortex.[6,26] Extensive mathematical analysis of cardiac rhythms in the USSR and abroad in the last 20 years have shown that this method reflects the state of regulatory mechanisms well, and that it may be widely used in the most diverse areas of medicine and physiology.[16,24] The lower the functional reserve of the corresponding systems, the higher the stress imposed on regulatory mechanisms in response to exertion. Exhaustion of functional reserves results in activation of controlling mechanisms at higher levels in order to mobilize the body's additional resources.[4,18] Since mathematical analysis of cardiac rhythms—spectrum analysis, in particular—enables the evaluation of the activity of different levels of control (autonomic, subcortical, cortical), it opens the possibility for evaluating the body's resistance to a given effect from cardiac rhythm. The automatic cardiac rhythm analyzers that have been created make it possible not only to measure the degree of stress on regulatory mechanisms from rhythm stability parameters, but also to delineate the slow-wave rhythm components of varying periods that characterize the activity of the corresponding levels of control.

The Ritm system consists of three units. It has (1) a unit for recording EKG and measuring RR intervals and (2) a unit for mathematical statistical treatment of changing series of values of cardiac interval duration. That unit's software makes it possible to conduct variational pulsometry, analyze transitional processes, and conduct spectrum analysis, thus enabling determination of the total intensity of the slow-wave components of cardiac rhythm in the ranges of 10 - 30 seconds (first-order waves), 30 - 80 seconds (second-order waves) and 80 seconds to five minutes (third-, fourth- and fifth-order waves). It also has (3) a unit for evaluating the functional state of the body. That unit can distinguish between the normal state, functional exertion, overexertion, and exhaustion of regulatory systems. Autonomic homeostasis, stability of regulation, and activity of subcortical nerve centers (determined from the ratio of intensities of respiratory and slow waves of the cardiac rhythm) are taken into account.[6] The slow-wave components of cardiac rhythm—third-order to fifth-order waves—are analyzed in the evaluation of psychophysiological state.[9]

Technically, the Ritm system is a microcomputer with a built-in EKG amplifying unit, an analog-to-digital converter, and a display for psychological testing. The software system supports analysis of changing series of cardiac intervals with preassigned programs and printout of the results.

Materials from mass prognostic examinations of essentially healthy people—industrial enterprise workers—show that the traditional clinical approach to data analysis and the use of only the parameters commonly accepted in clinical practice are not informative enough when the discussion turns from disease to functional states in the borderline zone between the norm and pathology. Figure 3 presents graphs of changes in the mean values of a number of cardiological indicators for persons of various ages in different functional states. Indicators such as pulse rate and arterial pressure vary negligibly in the prenosological and premorbid states (SAP does not exceed 145 mm Hg, PR does not exceed 75 per minute). Circulation stroke volume decreases noticeably only with advancing age. At the same time, a pronounced increase in exertion of regulatory systems is

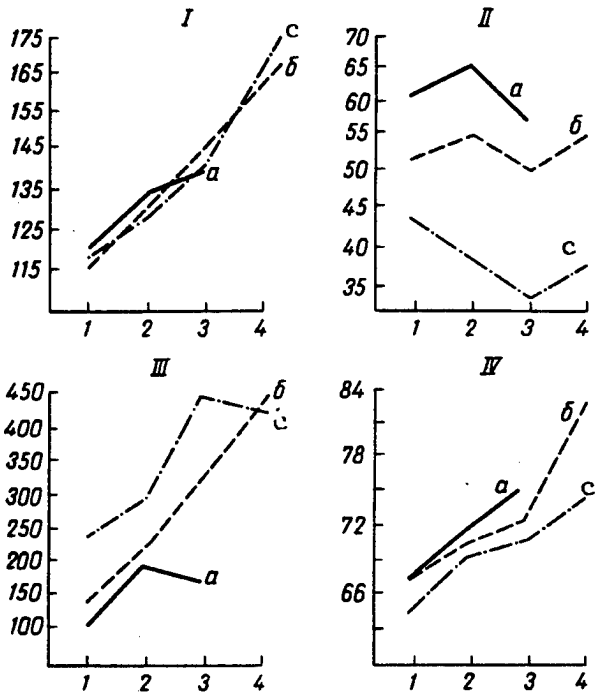

Figure 3. Dynamics of cardiological indicators in men of various ages in connection with change in body functional state: *x*-axis, functional state: 1—satisfactory adaptation, 2—functional stress, 3—unsatisfactory adaptation, 4—failure of adaptation; *y*-axis: I—systolic arterial pressure (mm Hg), II—stroke volume (in ml), III—index of exertion of regulatory systems (arbitrary units), IV—pulse rate, beats per minute. Age groups: a—25 or under, b—26-40, c—over 40

noted upon transition to premorbid states in the age groups of 25 - 40 and over 40.

The results of many years of cooperation between representatives of space and ground-based medicine have enabled the development of a scientifically sound design for a multipurpose, automated system for evaluating and predicting the body's functional states. The system is a logical continuation of the efforts begun with the creation of the Avtosan-82 mobile automated laboratory. It is a three-level system. The first level consists of the initial evaluation of functional state, identification of individuals in terms of level of health, and determination of the priority and urgency of further examination. The Kontrol system is an analog of the first level. The second-level system (Vita is its analog) is intended for diagnosis of functional states and determination of the probable profile of pathology. Specific objectives geared to adjusting or maintaining the level of health that is ascertained are carried out at the third level of examination. The examination program varies according to the group into which the patient is placed (healthy, essentially healthy, ill). For healthy people, the third level of the system is analogous to the Ritm system. If a high probability of a particular form of pathology is established, the examination at the third level is confined to a specific nosological specialization (cardiology, gastroenterology, surgery, etc.).

The proposed three-level, automated, multipurpose system is based on the principle of evaluating health as a certain capacity of the body to adapt to environmental conditions, and it may be used both in space medicine and in mass preventive examinations and mass health screening of the population. The structure and function of the system and its elements differ to a certain extent in each of those areas. In space medicine, where first-level systems are virtually absent (orbiting stations are involved), it is to that element that the greatest attention must be turned. A transition must be made from monitoring functional state in only the most critical flight phases (launch, reentry, EVA) to constant, comfortable and dependable monitoring that would make it possible to obtain dynamic information without which a constant prognosis of functional states cannot be made. The system's second and third levels as they pertain to space research may be improved by creating specialized questionnaires or introducing additional procedures that is possible to diagnose states specific to the conditions of a long flight.

The development of space poses new problems for mankind in science, engineering and technology. New problems also face medicine. The materials presented above show how intertwined ground-based and space problems are in the area of evaluating the functional states of healthy people. Space flights, the durations of which are increasing with every year, have been a powerful stimulus to the study of borderline states between health and disease—a new area in preventive medicine. In turn, the more than 10 years of experience of mass prenosological examination of various age, sex and professional groups[16] has been necessary for gaining a deeper theoretical understanding of the mechanisms responsible for the maintenance of the health in healthy people and for the development of new approaches to monitoring health. The proposed three-level system for evaluating and predicting functional states is one of the results of cooperation between space medicine and ground-based medicine. The embodiment of this design in the form of specific procedures and specific hardware will open up new possibilities for science to learn about the essence of health and disease.

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Standardizing the Quality of Viral Insecticides

917C0069 Moscow ZASHCHITA RASTENIY in Russian No 7, Jul 90 pp 8-9

[Article by M. G. Chukhriy, laboratory head, All-Union Scientific Research Institute of Biological Methods of Plant Protection]

[Text] The serious ecological situation on agricultural and forestry tracts requires increased production of biological plant-protection agents that are safe for people and the environment. Unlike other preparations, viral insecticides can control pest populations for prolonged periods, which is important considering pests can be passed from generation to generation. Research shows that baculoviruses, which are the basis for the preparations, are highly specific, that is, they infect only one or several closely related insect species, but do not infect beneficial insects.

Worldwide, more than 20 viral insecticides have been created and approved for production. However, their large scale production has not yet been organized. The manufacture of Elkar, intended for use against the cotton-boll worm, was set up in the United States, but it was halted in 1986 because the viral insecticide was not competitive with chemical preparations.

Improving the efficacy of biological preparations is an urgent problem for scientists. They can do that by finding strains that are more active, by improving the manufacturing processes for the production of insecticides, and by finding better preparation forms. To put it simply, there should be a guarantee that the promised efficiency will be attained. The viral insecticides that are produced should be of high quality and must meet specific criteria.

Unfortunately, such criteria have not yet been developed. Therefore, at the International Symposium on Microbial Pesticides, held in October 1988 in Plovdiv (Bulgaria), a commission called "Methods for Determining the Quality of Viral Insecticides" was created for developing a standard that would enable all specialists to use one and the same methodology to determine the quality of viral insecticides. May 1989 saw the commission's first meeting, in which it examined the first draft of a standard according to which viral insecticides must contain an infection that is capable of causing illness.

Thus, the first criterion is that the insecticide have a specific infectious potential. Also, it was suggested that the biological activity of the preparation, which characterizes the result of the action—the reaction of insects to it—be determined. That criterion is not so successful, because the activity is not a constant, and it depends upon a multitude of uncontrollable factors: cell-virus interaction, age of host-insect, etc.

The absence of the expected effect can also be explained by incorrect use of the viral agent: the source of infection is often inactivated by solar radiation or by an acidic or alkaline medium. Preparation quality can also change because of improper storage or the inactivation of the initial strain by other adverse factors.

Unfortunately, the production of viral insecticides at present involves the use of larvae from laboratory or natural populations of insects that are very difficult to control in terms of all the parameters needed to obtain stable strains of baculoviruses. In the USSR, the production of viral insecticides based on tissue culture cells is developing very slowly and is unprofitable because of the high cost of the culture media.

As for the mass breeding of insect-phytophages, a technology for producing cutworms has been developed, but it is difficult to breed large numbers of other pests in laboratory conditions. Because of that, researchers prefer to base the production of viral insecticides on the larvae of natural populations. That is exactly how large batches of viral insecticides are produced for use against larvae of gypsy moths (Virin-ENSh) and American white butterflies (Virin-ABB-ZK).

Evaluation of the viral material produced is a key aspect of production. For that purpose, the strain of baculovirus is determined with restriction analysis or morphometric methods, and the number of normal nucleocapsids—the infection source—is determined. Also determined is the amount of other microflora, which must be excluded by various methods. Thus, with infectious material that meets established criteria, it is fully possible to produce standardized, highly effective insecticides. This requires that regional biological laboratories organize the collection of larvae that have died from viral infections. Where possible, mass breeding of phytophages must be set up, as well as their infection and the production of a viral mass, which should then be sent for a quality check evaluation to production laboratories at science centers—for example, at the Biology Institute of the Latvian SSR Academy of Sciences, the All-Union Scientific Research Institute for Plant Protection, the All-Union Scientific Research Institute of Biological Methods of Plant Protection, the Ukrainian Scientific Research Institute for Plant Protection, the All-Union Scientific Research Institute for Microbiology (Novosibirsk), the Georgian Scientific Research Institute for Plant Protection (Tbilisi) and Central Asian Scientific Research Institute for Plant Protection—which are experienced in producing viral insecticides. It seems inadvisable to concentrate production of all viral insecticides in one place, as has been the case up to now. It seems sensible to organize their production in regions that are most favorable for breeding the various phytophage-hosts of baculoviruses upon which the preparations will be based. Certainly, standard viral insecticides can be produced only by specialized biotechnological laboratories with highly skilled specialists.

General Principles of Activation of Mast Cells by Cyclic Analogues of Basic Vasoactive Peptides

917C0033A Moscow BIOKHIMIYA in Russian Vol 55 No 6, Jun 90 (manuscript received 13 Feb 89) pp 988-994

[Article by Ye. A. Porunkevich, M. P. Ratkevich, G. G. Kublis, F. K. Mutulis, and G. I. Chipens, Institute of Organic Synthesis, LaSSR Academy of Sciences, Riga]

UDC 577.175.8

[Abstract] The histamine-liberating activity of linear and cyclic analogues of bradykinin and kallidin was studied in rat peritoneal mast cells and structure-activity relationships investigated. Fixation of the spatial structure of the molecule and simultaneous neutralization of the C-terminal carboxylic acid group in the cyclic bradykinin analogues led to increased histamine release effectiveness. Increasing basicity of the peptide on reduction of the lost basic group also strengthened histamine-liberating activity. Replacement of the C-terminal phenylananine or arginine by leucine decreased activity. Receptor binding studies demonstrated that, under the experimental conditions used, linear bradykinin and angiotensin did not displace a labeled cyclic analogue of high affinity, while unlabeled analogue, the cyclic analogue of bradykinin, polymixin B and substance 48/80 did demonstrate displacement. Comparison of results for angiotensin, bradykinin and kallidin indicated that cyclization, increased basicity and increased hydrophobicity increased histamine-liberating activity in all three peptides. Formation of fixed adjacent hydrophobic and hydrophilic zones appears to play an important role in the interaction of the compounds with the lipophillic portion of the cell membrane. At least a six-residue ring and at least one or two terminal basic amino acids are necessary for activity. The cyclic and linear analogues appear to interact with different receptors. The results obtained for the cyclic peptides were independent of the pharmocological activity of their linear analogues. Figures 2; references 11: 7 Russian, 4 Western.

Bioluminescence System of Fireflies. Interaction of Oxyluciferin and Analogue Reaction Products With Luciferase as Measured by Fluoresence Spectroscopy

917C0033B Moscow BIOKHIMIYA in Russian Vol 55 No 6, Jun 90 (manuscript received 22 Mar 89) pp 1052-1058

[Article by O. A. Gandelman, L. Yu. Brovko, N. N. Ugarova, and A. A. Shchegolev, Moscow State University imeni M. V. Lomsomov]

UDC 577.158.54

[Abstract] In order to elucidate the nature and structure of the products of the luciferin-luciferase reaction, the fluorescence spectra of oxyluciferin (OL), luciferin (L), 6'-methoxyluciferin (MeOL), and 2-CN-6'-OH-benzthiazol (BT) and their enzyme complexes were studied at pH 1 - 10 in water and aqueous methanol. For OL, L, and BT, which have a free 6'-OH group, the transition from basic to neutral pH was accompanied by shifts in the absorption maxima to shorter wavelengths. In ethanol, independent of effective pH, all the compounds had one characteristic absorption maximum in the shortwave region, corresponding to the protonated form. The pK of the 6'-OH group of L and OL in the excited state was found to be -0.5, indicating that the 6'-OH is deprotonated at all pHs in the excited state. Excitation of a L molecule with a protonated COOH-group appears to be the source of the red fluorescence observed with L. Fluorometric titration of L, OL, and BT with excess enzyme did not alter the form or intensity of their fluorescence spectra. Dissociation constants were 11 μM, 1.5 μM, and 13 μM respectively. The results suggest that the 6'-OH is not immersed in the hydrophobic pocket of the enzyme, so that the fluorophor desorbs on excitation and resorbs after light emission. The fluorescence spectra of chromatographically isolated enzyme-product complex confirms this suggestion. Only the enol form was observed, possibly due to stabilization by an electrophilic amino acid. The fluorescence spectrum of OL is strongly dependent on its microenvironment. The spectrum of bioluminescence was closest to that of free OL in water. This supports the concept that excitation causes dissociation of the enzyme-OL complex. After light emission, the product binds to a different site on the enzyme. The reaction is accompanied by strong conformational changes in the enzyme protein. Figures 4; references 21: 5 Russian, 16 Western.

Cyclic AMP as Possible Mediator of Formation of Immune Response of Plant Cells, Induced by Eikosanoides

917C0048B Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 313 No 4, Aug 90 pp 996-998

[Article by O. Yu. Ocheretina, L. I. Chalova, K. A. Karavayeva et al.; Institute of Physiology imeni I. P. Pavlov; USSR Academy of Sciences; Scientific Research Institute of Experimental Medicine; USSR Acadamy of Medical Sciences; Leningrad]

UDC 632.938+577.57.053.4

[Abstract] A study of Temp variety potato tubers used, as an inductor of prolonged resistance of potato tuber tissue to the phytofluorosis pathogen, arachidonic acid in a 10^{-7}M concentration which increased tuber tissue resistance to phytofluorosis and in a 10^{-7}M concentration which caused necrotization of the tissues and accumulation of phytoalexins in them. Spraying the whole tuber with arachidonic acid immunized the tuber. Radioisotopic dilution revealed the presence of cyclic nucleotides in the tuber tissues (30.2 - 40.1 pmoles of cAMP and 14.0 - 15.2 pmoles of cGMF) to 1 g of raw tissue. Treating the

tubers with arachidonic acid changed the cyclic nucleotides level in the point of growth of the tissues and the underlying parenchyma. The high necrosis-forming concentration of arachidonic acid (10^{-4}M) greatly reduced the level of both nucleotides. An immunizing concentration (10^{-7}M produced, in the first hours after treatment, an increase of level of cAMP and an insignificant inhibition of the cGMP level. Within 24 hours the effect of immunization with respect to the cyclic nucleotides smoothed out and the level of both nucleotides approached the control level. The data showed the greater role of cAMP than cGMP in the immunization process. The study showed that the physiological action of eicosanoids changes the cyclic nucleotides system in plants including a change of activity of their metabolism and a change of the level of the nucleotides themselves, espcially that of cAMP. This suggested consideration of the cAMP system as a possible intracellular mediator of the effect of eicosanoids in plants. References 13: 6 Russian, 7 Western.

Interaction of Toxin of Sea Anemone Radianthus Macrodactylus With Bilayer Phospholipid Membranes

917C0070A Moscow BIOLOGICHESKIYE MEMBRANY in Russian Vol 7 No 7, Jul 90 pp 763-769

[Article by A. N. Chanaturiya, O. Ya. Shaturskiy, V. K. Lishko, M. M. Monastyrnaya and E. P. Kozlovskaya, Institute of Biochemistry imeni A. V. Palladin, Ukrainian Academy of Sciences, Kiev; Pacific Institute of Bioorganic Chemistry, Far-Eastern Department, USSR Academy of Sciences, Vladivostok]

UDC 577.352.2:615.919

[Abstract] It was previously determined that the toxin from the sea anemone *Radianthus macrodactylus,* which has hemolytic activity, forms ioicn channels in bilayer phospholipid membranes. This article continues studies of the interaction of the toxin with bilayer membranes. A number of factors influencing insertion of the toxin in bilayer membranes are investigated, and it is shown that bonding of bivalent cations with the membrane facilitates insertion of the toxin. There is a critical temperature, below which channels are not formed. The influence of potential on channel conductivity is investigated and it is shown that at potentials over 40 mV, the channels become closed. It is assumed that the decrease in conductivity with increasing potential is determined by the fraction of channels which are closed. Figures 6; references 19: 12 Russian, 7 Western.

Structure-Activity Models of Organophosphorus Cholinesterase Inhibitors

917C0160A Moscow BIOORGANICHESKAYA KHIMIYA in Russian Vol 16 No 11, Nov 90 (manuscript received 19 Jan 90) pp 1509-1522

[Article by O. A. Rayevskiy, V. V. Chistyakov, R. S. Agabekyan, A. M. Sapegin and N. S. Zefirov, Institute of Physiologically Active Substances, USSR Academy of Sciences, Chernogolovka, Moscow Oblast]

UDC 577.2.311.042

[Abstract] A discriminant, cluster and regression analysis was carried out on 240 phosphoryl and thiophosphoryl inhibitors of human erythrocytic acetylcholinesterase (EC 3.1.1.7) and equine serum butyrylcholinesterase (EC 3.1.1.8) in order to define structure-activity parameters. The results demonstrated that 15 key descriptors provided a sufficient database for classification of some 98 percent of the compounds. The wide range of values for K_d and k_p for irreversible inhibitors and of K_i for reversible inhibitors confirmed the importance of substituents on the P atom for inhibition. The results also provided a predictive model system for novel cholinesterase inhibitors. Tables 3; references 57: 42 Russian, 15 Western.

Interaction of Pyruvoyl Amino Acid With Protonic Solvents

917C0160B Moscow BIOORGANICHESKAYA KHIMIYA in Russian Vol 16 No 11, Nov 90 (manuscript received 03 Jan 90; in final form 19 Mar 90) pp 1563-1566

[Article by R. D. Lampeka, I. O. Fritskiy, Kiev State University imeni T. G. Shevchenko]

UDC 547.466'484.22:543.422.25

[Abstract] NMR studies were conducted on pyruvoylglycine, pyruvoyl-L-alanine and pyruvoyl-L-methionine in protonic (water, methanol) and aprotic (dimethyl sulfoxide) solvents to assess solvation of these potential ligands that may be used in modeling metal-peptide interactions. Analysis of ^{13}C-NMR spectra in both solvent types revealed considerable differences, with the appearance of a ca. 95 ppm signal in the protonic solvents. The latter signal was attributed to addition of a water or methanol molecule to the keto group of the pyruvoyl fragment, i.e., to solvation of the C atom of the 2-carbonyl group. In addition, a ca. 197 ppm signal, representative of an unsolvated keto group, indicated that the two forms exist in a dynamic equilibrium. Finally, information provided by ^{1}H-NMR spectra showed that at equilibrium ca. 40 percent of the species are solvated. Figures 2; references 7: Western.

Crustacean-Specific Neurotoxin From Spider Latrodectus Mactans Tredemcimguttatus

917C0160C Moscow BIOORGANICHESKAYA KHIMIYA in Russian Vol 16 No 11, Nov 90 (manuscript received 29 Jun 90) pp 1567-1569

[Article by V. G. Krasnoperov*, O. G. Shamotchenko and Ye. V. Grishin*, Institute Bioorganic Chemistry

imeni M. M. Shemyakin, USSR Academy of Sciences, Moscow, and *Pushchino Branch of the Institute, Moscow Oblast]

UDC 577.112.088.3:591.145.2-544

[Abstract] Conventional ion exchange chromatography on Mono Q and Mono S (Pharmacia) columns and hydrophobic chromatrography on Phenyl-Superose columns led to the isolation of a crustacean-specific neurotoxin from the venom of spider Latrodectus mactans tredemcimguttatus. The 120 kD neurotoxin has been designated α-latrocrustotoxin. Testing on one-year-old crayfish Procambarus cubensis and Astacus astacus (suborder Decapoda) by injection into the pericardial area yielded an LD_{50} value of ca. 100 μg/kg. In the case of the river shrimp Gammarus locusta (suborder Amphipoda) the LD_{50} for α-latrocrustotoxin was approximately an order of magnitude greater. Finally, α-latrocrustotoxin was found to be nontoxic for Galleria mellonella moths and Balb/c mice in doses of ca. 5 mg/kg. Figures 2; references 4: Western.

Synthesis of Human Interkeukin-1α by Polymerase Chain Reaction Amplification of mRNA-cDNA Duplex

917C0160D Moscow BIOORGANICHESKAYA KHIMIYA in Russian Vol 16 No 11, Nov 90 (manuscript received 29 Jun 90) pp 1570-1573

[Article by Ye. N. Lebedenko, O. V. Plutalov and Yu. A. Berlin, Institute of Bioorganic Chemistry imeni M. M. Shemyakin, USSR Academy of Sciences, Moscow]

UDC 577.214.3

[Abstract] Synthesis of human interleukin 1α (IL-1α) was attained by using the polymerase chain reaction (PCR) to amplify a mRNA-cDNA duplex obtained by reverse transcription of total adenylated mRNA isolated from human monocytes. Using the technique developed by Brenner et al. [Brenner, CA, et al., BioTechniques, 7(10): 1096, 1989], and a downstream primer corresponding to the 3'-end and an upstream primer representing the 113 - 271 amino acid sequence of mature IL-1α, resulted in the synthesis of the IL-1α gene. Subsequent cloning of the gene in plasmid pUC19 and sequencing studies led to demonstration that the cloned IL-1α gene contained initiation and termination codons. This approach to gene reconstruction obviates the need for the synthesis of the corresponding double-stranded cDNA commonly used in PCR, relying instead on the primary product of reverse transcription of unfactionated mRNA. Figures 1; references 9: 1 Russian, 8 Western.

Synthesis of Phosphothiolate Analogs of Oligoriboadenylates Using Salicyl Chlorolophosphite

917C0160E Moscow BIOORGANICHESKAYA KHIMIYA in Russian Vol 16 No 11, Nov 90 (manuscript received 17 Jan 90) pp 1537-1544

[Article by Ye. I. Kvasyuk, T. I. Kulak and I. A. Mikhaylopulo, Institute of Bioorganic Chemistry, Belorussian SSR Academy of Sciences, Minsk]

UDC 546.183:546.22:577.113.6

[Abstract] A series of thiophosphate analogs of (2'-5') oligomers of adenylic acid were synthesized by using salicyl chlorophosphite for the formation of internucleoside phosphodiester bonds. The purpose was to provide additional analogs that may be useful in furthering an understanding the action of interferon. The method was found suitable for the concomitant synthesis of the following (2'-5') and (3'-5') thiophosphates, albeit in low yields (2.4 - 8.6 percent): adenylyl(2'-5')adenosine, adenylyl(3'-5')adenosine, adenylyl(5'-5')adenosine, adenylyl(2'-5')-P-thioadenylyl(2'-5')adenosine and adenylyl(2'-5')-P-thioadenylyl(3'-5')adenosine. The (2'-5') and (3'-5') dimers were obtained as individual R_p and S_p diastereoisomers. Synthesis of these compounds was confirmed by snake venom hydrolysis and UV, CD and ^{1}H-NMR spectroscopies. References 26: 6 Russian, 20 Western.

Neurochemical Correlates of Cortical-Subcortical Interrelationships in Activation of Dopaminergic System With L-DOPA

917C0171B Moscow ZHURNAL NEVROPATOLOGII I PSIKHIATRII IMENI S.S. KORSAKOVA in Russian Vol 90 No 10, Oct 90 (manuscript received 03 Mar 89) pp 68-71

[Article by L. M. Gershteyn, A. V. Sergutina, S. A. Titov and T. L. Chebotarev, Brain Institute, USSR Academy of Medical Sciences, Moscow]

UDC 616.831-008.61:577.175.823]-076.4

[Abstract] The neurochemical backround underlying baseline motor activity in open-field trials was studied on 240 - 270 g male Wistar rats following activation of the dopaminergic system with exogenous madopar-125. The study revealed that in the case of the high-activity (HA) rats the levels of aminopeptidase (AP), glutamate dehydrogenase (GDH) and glucose-6-phosphate dehydrogenase (G6P DH) activities in layers III and IV of the sensorimotor cortex, caudate nucleus, and n. accumbens septi were greater than in the low-activity (LA) rats. Intraperitoneal administration of 25.5 mg/kg of medopar-125 (equivalent to 50 mg/kg of L-DOPA) for 14 days led to a reduction in motor activity in both groups of animals, but the reduction in the HA animals was much more pronounced both in the presence and

absence of stress. In the case of the HA animals the greatest neurochemical changes occurred in n. accumbens septi with an increase in G6P DH of 33 percent and an increase in cytoplasmic protein of 54 percent. In LA rats changes in n. accumbens septi were insignificant. The most impressive changes in the latter animals were noted in layer V of the sensorimotor cortex, consisting of a 37 percent reduction in cytoplasmic protein and a 19 percent reduction in AP activity. In addition, in layer III in LA rats structural cytoplasmic proteins increased by 46 percent in combination with a 16 percent reduction in AP activity. These findings provide an indication that changes in motor activity in conjunction with activation of the dopaminergic system involve alterations in 'plastic' and oxidative metabolism of the brain. Figures 3; references 11: 9 Russian, 2 Western.

Concerning Possibility of Significant Reduction of Defibrillation Current After Proper Selection of Moment of Applying Defibrillating Pulse. Mathematical Model

907C0849B Moscow BIOFIZIKA in Russian Vol 35 No 3, May-Jun 90 pp 500-503

[Article by A. M. Pertsov, V. N. Biktashev, Ye. A. Yermakova and V.I. Krinskiy; Institute of Biological Physics; USSR Academy of Sciences; Pushchino (Moscow Oblast); Scientific Research Computer Center; USSR Academy of Sciences]

[Abstract] A study of the effect of defibrillating pulses on arrythmias associated with the rise of re-entries (leading cycles), simulated on an electronic computer, showed that the defibrillation threshold may vary 2- to 4-fold, depending upon the time of application of a pulse. Arrythmias caused by different numbers of leading cycles (from 1 - 18) were investigated. The study employed a model in the form of a 2-dimensional layer of cells each of which was connected with four neighboring cells. Ionic currents of each cell were described by a system of two differential equations. Defibrillator pulses were modelled by a 10 ms current, fed simultaneously to all cells of the layer. In case of functionally determined re-entry (leading cycles), the defibrillation mechanism differed fundamantally from the generally accepted mechanism and involved a shift of the leading cycles beyond the limits of the excited tissue and mutual elimination of leading cycles with opposite direction of rotation. The defibrillation mechanism presupposes homogeneous depolarization of the tissue but requires lesser amplitudes of current. Currents only several times higher than threshold currents were adequate. The main condition of effectiveness of such low-amplitude defibrillation was proper selection of the moment of application of the pulse and the interval between pulses when using a series. The model used was greatly simplified and provided only a qualitative description of phenomena occurring in the myocardium. Figures 5; references 10: 5 Russian, 5 Western.

Toward Theory of Resonance in Excitable Media

907C0849C Moscow BIOFIZIKA in Russian Vol 35 No 3, May-Jun 90 pp 504-508

[Article by A. Yu. Abramychev, V. A. Davydov and A. S. Mikhaylov; Department of Physics; Moscow State University imeni M. V. Lomonosov]

[Abstract] The resonance of spiral waves in a heterogeneous and non-steady excitable medium with a periodically changing gradient of its parameters was studied within the framework of a kinematic approach to the description of autowave processes. Resonance of the scroll rings during periodic change of the medium was also studied. The possibility of controlling the collapse or expansion and the drift of the ring as well as its stabilization was demonstrated. Figure 1; references 11: 10 Russian, 1 Western.

Model of Chemical Memory of Neuron

907C0849D Moscow BIOFIZIKA in Russian Vol 35 No 3, May-Jun 90 pp 518-519

[Article by Yu. Z. Saakyan and L. Ye. Tsitolovskiy; Moscow Institute of Radiotechnology, Electronics and Automatics]

[Abstract] A mathematical model of chemical memory of a neuron which reduces the number of substances required for recognition of a signal was described and discussed. Chemical bonds formed between simultaneously excited synapses as a result of reactions occurring in the cell. All reactions described by the system of equations may proceed simultaneously in the cell. The most frequently encountered combinations of simultaneously activated synapses have interconnected chemical bonds and neuron excitability grew upon recognition of a rewarded signal and generation of an action potential was facilitated. The neuron excitability decreased for unrewarded signals. Conclusions concerning the model were confirmed, especially those concerning problems of associativity of the memory and recognition of images. References 2: Western.

Effects of Ultraviolet Light on Bacteriorhodopsin

917C0100C Moscow RADIOBIOLOGIYA in Russian Vol 30 No 4, Jul-Aug 90 pp 506-511

[Article by L. S. Broun, A. A. Kononenko, T. B. Prptaspva, I. B. Fedorovich and S. K. Chamorovskiy, Biological Faculty, Moscow State University; Institute of Chemical Physics, USSR Academy of Sciences, Moscow]

UDC 577.391.612.014.44

[Abstract] An analysis was conducted on the effects of UB-B light (280 - 320 nm) on bacteriorhodopsin (BR) isolated as purple membrane suspension from H. halobium 353-P, in view of the potential applications of BR in biotechnology. Analysis of the spectral changes showed that at UV-B doses = / < 15 kJ/m^2 induced a bathochromic shift in the major absorption band, while at > 15 kJ/m^2 destruction of the chromophoric groups led to bleaching of the α (major) and γ (UV) bands resulting in the appearance of a new absorption band at 340 - 380 nm. Subsequently, the latter band also disappeared. Dehydration was shown to decelerate the process of UV-B mediated destruction of BR. Since BR fluorescence is primarily due to tryptophanyl residues, the bathochromic shift was attributed to ionization of two of these moieties. Figures 4; references 25: 2 Russian, 23 Western.

Site-directed Mutagenesis in Higher Plants Through Homologous Recombination

907C0843C Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 312 No 6, Jun 90 pp 1505-1507

[I. F. Kanevskiy, M. Tsoko, L. Marton and Yu. Yu. Gleba; Department of Cell Biology and Engineering; Institute of Botany imeni N. G. Kholodniy; UkSSR Academy of Sciences; Kiev; Institute of Plant Physiology; Biological Research Center; Hungarian Academy of Sciences; Seged]

UDC 575:579.252

[Abstract] Results concerning modification of genes in higher plants in situ, mediated by integration of transforming DNA in a locus-target by means of homologous recombination were presented and discussed. Previously produced transgenic tobacco Nicotiana plumbaginifolia plants, containing, in their genome, one copy of TR-DNA plasmid pTiAch5 Agrobacterium tumefaciens, three genes of which encode enzymes for mannopin and agropin synthesis, were used as recipients for repeated transformation and Tr-DNA served as the target for recombination. The study resulted in development of a model system for the study of mechanisms of site-specific integration of allogenic DNA in the genome of the plants via homologous recombination. The use of the system of transformation of plant cells with use of agrobacteria made it possible to mutate or correct defects of genes with a frequency of nearly 1 percent without selective pressure in favor of the recombinants. Figures 3; references 15: 1 Russian, 14 Western.

Baculovirus System of Expression of Fire-Fly Luciferase in Bombyx Cells

907C0843D Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 312 No 6, Jun 90 pp 1507-1510

[Article by T. N. Kopylova-Sviridova, T. V. Gorelova, V. I. Krauzova et al.; Institute of Biochemistry and Physiology of Microorganisms; USSR Academy of Sciences; Pushchino; Moscow Oblast; Institute of General Genetics; USSR Academy of Sciences; Moscow]

UDC 575:616.912-085.371:616.36-002

[Abstract] The article presented results concerning expression of the gene of luciferase Photinus pyralis in insect cells with the use of the promising, in biotechnology, vector-virus of nuclear polyhedrosis of Bombyx cells (BmNPV), belonging to the family of baculoviruses. Stable recombinant clones of baculovirus which possess high luciferase activity were produced. These clones may be used to study reproduction of viruses, using a rapid and sensitive method of bioluminescence detection. Figures 4; references 9: Western.

Development of Semiautomatic Enzymatic Glucose Analyzer for Control of Process of Antibiotic Biosynthesis

917C0044A Moscow ANTIBIOTIKI I KHIMIOTERAPIYA in Russian Vol 35 No 6, Jun 90 (manuscript received 6 Oct 89) pp 12-18

[Article by V. I. Kranyauskas, S. B. Itsygin, V. A. Nesterov, P. V. Choban, V. G. Murygin, Yu. E. Bartoshevich, and E. V. Palis, "Ferment" Scientific Production Organization, Vilnius; All-Union Scientific Research Institute of Antibiotics, Moscow]

UDC 615.33.012.6.07

[Abstract] A laboratory-scale glucose analyzer based on an enzyme electrode was developed for controlling the process of antibiotic biosynthesis. Due to the presence of substances in the culture fluid to be analyzed which interfere with the measurement of the hydrogen peroxide product, the system used oxygen level determination. Fluoroplastic electrotechnical film, thickness 5 or 10 υm, was chosen for the gas-permeable membrane of the oxygen electrode. It was determined experimentally that it was necessary to thermostat the electrode and that linear agitation velocity should not exceed 0.30 m/sec. A 10 υm Dacron membrane with 200 nm pores was found to give the best protective dialysis membrane. A glucose-measuring instrument was constructed, using FM-11 glucose oxidase membrane, and its sensitivity found to be maximal at 50. Sensitivity was independent of pH in the 5.5 - 7.0 range. Signal was linear with glucose concentration from 0 - 0.05 percent. The glucose-measuring instrument was incorporated in a prototype device, which was capable of performing 20 tests per hour. Since the enzyme membrane time to failure varied from 7 - 45 days, membrane replacement once a week is recommended. The prototype was tested by comparison with results of chemical determinations of glucose levels in a rifamycin-synthesizing culture. In the 1 - 10 percent glucose range, the difference between the results of the two methods was about 5 percent. Below 1 percent glucose the chemical method gave higher results, due to the presence of interferences. The prototype was also tested in systems containing glucose, lactose, sucrose, complex carbohydrates and corn meal as carbohydrate sources. Levels down to 0.02 - 0.4 percent could be measured. The device developed may be profitably applied to the control of antibiotic biosynthesis. Figures 6; references 14: 3 Russian, 11 Western.

Isolation of Crimean Hemorrhagic Fever Virus From Blood of Farm Animals

917C0060B Dushanbe ZDRAVOOKHRANENIYE TADZHIKISTANA in Russian No 3, May-Jun 90 pp 75-77

[Article by Z. Ye. Gordeyeva, M. A. Kostyukov, O. I. Vyshemirskiy and T. V. Volkova; Tadzhik Scientific Research Institute of Epidemiology and Hygiene]

[Abstract] A report of isolation of Crimean hemorrhagic fever virus from farm animals was based on a study of 150 blood samples (100 from cows and 50 from sheep) collected at Dushanbe Meat Combine. Virusological study of the blood samples revealed six viral agents (four from cow blood and two from sheep blood). The incubation period after primary infection was 6 - 9 days. The clinical picture of the disease included convulsions, paralysis of the extremities and death. All isolated strains were sensitive to ether. This was the first case of isolation of Crimean hemorrhagic fever virus in the USSR (in Tadzhikistan) from the blood of animals brought from Gissarskiy and Leninskiy rayons in which this disease is endemic. The findings reconfirmed the role of farm animals in Crimean hemorrhagic fever not only as supporters of Crimean hemorrhagic fever but also as carriers of the virus. References 6: Russian.

Book on Infectious Diseases in Ukrainian SSR

917C0065B Kiev VRACHEBNOYE DELO in Russian No 7, Jul 90 p 124

[Review by A. A. Keller of book "The Risk of Infection of the Population with Siberian Ulcer, Tetanus, Ascaridosis, Tularemia, and Leptospirosis in the Ukrainian SSR: An Atlas", edited by Prof. K. M. Sinyak, Kiev, "Geodezist" Cooperative, 1989, 25 volumes]

UDC 616.9(084)(477)(049.3)

[Text] In the present stage of development of thematic cartography, systematic treatment of the epidemic process under the aspect of epidemiological geography helps bring out new sociobiological factors of influence on the spatio-temporal characteristics of this process. Systemic cartography, based on thematic cartography, makes it possible not only to utilize current knowledge about the surrounding world in the investigative process, but also to create new graphic forms thereof. Stylized-surface maps have proved to be promising, including field-of-event maps, which make it possible to depict in models the characteristics of symptoms in the form of continuous quantities. This type of cartographic model was used by the authors in creating the atlas; what is new is its thematic orientation.

The publication of the first atlas of risk of infection and invasion is a relatively new trend in the development of epidemiological-geographical studies in the Ukraine. The creation of nosogeographical maps of individual oblasts of the Ukrainian SSR is urgent in connection with heightened interest from the public in maps reflecting the living conditions and state of health of people. Therefore, the presentation of maps of Siberian ulcer, tetanus, ascaridosis, tularemia, leptospirosis, assembled in separate volumes for the oblasts of the Ukrainian SSR, is timely and essential. Each of the 25 volumes of the atlas (corresponding to the oblasts of the Ukrainian SSR) contains severe thematic maps reflecting the nosological forms.

Given the concept of the team of authors that the risk of infection consists in the probability of infectious and invasive pathogens getting into the organism of the host and retaining their biological properties therein, the nosogeographical maps were compiled from the results of monitoring observation of the conditions of viability of pathogens in objects of the environment, as well as data of recorded cases of illness for the nosological forms. The duration of the observations and the extent of the territory of investigation enabled an objectification of the scientific inferences in the form of maps of risk of infection for each oblast and for the Ukrainian SSR as a whole.

Such a trend in research has been widely debated at the meetings of scientific societies and reflected in more than 40 publications devoted to the use of medical geography in the cartography of epidemic processes. This has helped in the broad practical adoption of nosogeographical maps. During the course of preparation, fragments of the atlas were shown at the USSR VDNKh and scientific conferences, which allowed the broad circle of specialists to become familiarized in advance with the scientific concept of the authors and to give their approval of it.

The authors of the atlas, in addition to showing the morbidity of the population at points of recording cases of disease, making use of the method of field-of-density maps for the particular phenomena as elaborated by V. A. Chervyakov (taking into account cases of disease at population centers), have created a series of maps reflecting the continuous, not discrete, distribution of the phenomena over the territory. These data are especially important in systems of research maps, which are important for study of the factors of formation of natural-focus and epidemic diseases. The use of the method of field-of-density maps of the studied symptoms enables a study of the correlation connections between the diseases and the living and working conditions of the people (social factors), as well as natural phenomena. On the basis of the interrelationships identified, system-forming natural factors are picked out, the distribution of which is also reflected in the maps of the atlas. Consequently, consideration is given to the ecological characteristics of the territory which influence human economic activity, change in which reveals active influence on the pathogens of infections and invasions. The direct connection between human economic activity and the agrochemical characteristics of the soils of the territories, as well as their influence on the survivability of the pathogens, makes it possible to assign the soil properties to the rank

of a system-forming factor responsible for the harboring of infections that live in the soil—Siberian ulcer, tetanus, and ascaridosis.

On the basis of the relationships discovered, prognostic morbidity maps—maps of the risk of infection—were created and the degree of realization of the prognosis was determined. It is therefore possible to recommend the use of the maps for risk of infection by Siberian ulcer, tetanus, ascaridosis, tularemia and leptospirosis as a scientific foundation in development of a system of preventive measures in the various administrative and natural regions of the Ukrainian SSR. Use of the atlas will allow better effectiveness of these measures when carrying out broad-scale economic plans that involve population migration. Furthermore, the high scientific stature of the atlas warrants the recommendation that the findings be adopted in public health practice for prevention of diseases and as a methodological tool in compilation of maps for other nosological forms.

The publication of the atlas should be looked upon as a scientific cartographical production that reflects the transition of epidemiological geography to a qualitatively new level—quantitative analysis of the interrelationships between environmental conditions and human health.

Lyme Borreliosis in Lithuania: Its Spread, Clinical Picture and Effectiveness of Its Treatment

917C0074A Moscow ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII in Russian No 7, Jul 90 (manuscript received 17 May 89) pp 19-23

[Article by L. I. Moteyunas, A. R. Shadzhene, S. V. Tumosene, M. I. Kalinin, S. V. Deuyetas and G. K. Regalene, Vilnyus University; Kaunas Clinical Hospital for Infectious Diseases; Scientific Research Institute of Epidemiology and Microbiology imeni N. F. Gamalei, USSR Academy of Medical Sciences, Moscow]

UDC 616.98:579.834.114]-036.22(474.5)

[Abstract] In 1988 there was a reported incidence of 376 cases of Lyme borreliosis (LB) in Lithuania. This included 101 cases with the first stage of circular migrating erythema. Specific antibodies to the causative agent of LB were detected in 40 patients (39.6 percent) of this group. All 101 LB patients were intensively treated with antibiotics for 10 - 14 days. The effectiveness of this treatment was evaluated 4 - 5 months later. Data were collected on only 90 patients, including 82 who had undergone treatment. Complete recovery was evident in 52 cases (63.4 percent). Twenty other subjects regarded themselves to be practically healthy. In 10 patients (12.2 percent), however, the disease continued active (this included six patients who had stopped the prescribed course of treatment by their own volition). Among eight patients who had not yet started treatment, five had apparent indications of progress of the disease. Information on the incubation period of the disease and its seasonal character is given, as well as on the characteristic features of erythema and concomitant symptoms. References 13: 7 Russian, 6 Western.

Spread of Hepatitis B Virus Infection in Family Foci in Territory Hyperendemic for Hepatitis B

917C0074B Moscow ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII in Russian No 7, Jul 90 (manuscript received 18 Jan 89, after revision 16 Jun 89) pp 27- 31

[Article by R. A. Rakhimov, Uzbek Affiliate, Virology Institute imeni D. I. Ivanovskiy, USSR Academy of Medical Sciences, Tashkent]

UDC 616.36-002.1-022:578.891]-036.21-07

[Abstract] Epidemiological surveillance with the use of highly sensitive procedures for the indication of hepatitis B (HB) virus infection markers in their dynamics revealed that in a territory hypersensitive for HB, in addition to the existing high risk of this infection as a result of parenteral medical procedures, the intensive natural transmission of HB virus infection transpires under conditions of everyday contact with infectious sources, patients with chronic forms of HB virus infection being of the greatest epidemic importance. Under these conditions, children up to age seven were found to be in the highest risk category. Accordingly, children in this age group must henceforth be subjected to specific preventive measures against HB. The spread of the HB virus infection epidemic process within family units is usually manifested in anicteric (usually undiagnosed) forms of this disease. These and other circumstances make it necessary to develop appropriate antiepidemic and prophylactic measures practicable in hepatitis B foci. References 12: 10 Russian, 2 Western.

Paratyphoid Morbidity in Uzbek SSR

917C0074C Moscow ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII in Russian No 7, Jul 90 (manuscript received 21 Sep 89) p 115

[Article by M. V. Nevskiy, L. A. Savitskaya, Z. M. Aminzade and I. Kh. Mamatkulov, Tashkent Scientific Research Institute of Epidemiology and Infectious Diseases, Ministry of Health, Uzbek SSR]

UDC 616.927.7-036.2:312.6(575.1)

[Abstract] During recent years paratyphoid infections in the USSR have been a major problem only in some of the republics of Central Asia. During the period 1983 - 1986 in the Uzbek SSR, for example, there have been from 7.5 - 13 cases per 100,000 population versus 2 per 100,000 for the USSR as a whole (the reported incidence is even much higher in the Tajik SSR and the Turkmen

SSR). In the Uzbek SSR 68 - 98 percent of these cases are paratyphoid B. The disease often transpires in a very light form and in many cases there is an inconsistency between clinical manifestations and laboratory tests. Due to inadequate testing, those exhibiting a symptom complex caused by S. java have been incorrectly diagnosed as suffering from paratyphoid B. This high reported incidence of paratyphoid B in the Uzbek SSR is therefore attributable, to a considerable degree, to an incorrect interpretation of bacteriological tests. The problem is that an identical response reaction is caused by both S. java and S. schottmuelleri. A diagnosis of paratyphoid B will be valid only when there are clinical manifestations of the disease and it is established that the symptom complex is not attributable to S. java. In the Uzbek SSR, therefore, there is an artificial exaggeration of the number of cases of paratyphoid B due to the incorrect biochemical differentiation of S. schottmuelleri and S. java. It is possible that the very same situation prevails in other republics of Central Asia with an extremely high hyperdiagnosis of this infection.

Spread of Viral Hepatitis B in Chronic Hemodialysis Department

917C0074D Moscow ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII in Russian No 7, Jul 90 (manuscript received 16 May 89) pp 116-117

[Article by V. V. Nechayev, A. S. Pevzner, O. S. Ulyanova, S. L. Mukomolov and V. S. Vysotskiy, Leningrad Sanitary-Hygienic Medical Institute]

UDC 616.98:578.891]-022.369-036.2-07

[Abstract] The incidence of viral hepatitis B in the Chronic Hemodialysis Department was investigated thoroughly to ascertain the reasons for its spread among patients and hospital workers. The various criteria used in this investigation are discussed. Contamination occurred not only during the transfusion of slightly infected donor blood and during hemodialysis sessions, but also during movement of small doses of virus during different parenteral interventions from patients carrying the virus to susceptible patients and hospital personnel. The epidemic viral hepatitis B process in the department transpires intensively but primarily latently and is not readily monitorable within the framework of current sanitary practices and therefore these procedures for preventing contamination require revision. The epidemiological monitoring system must include measures for examination of patients by clinical-biochemical methods from the moment of their admission, checking of all donor blood (which was found to be the causative agent in many cases) using highly sensitive tests, and other procedures such as prophylactic inoculations, sanitary and hygienic measures.

Clinical Classification of AIDS

91WE0092X Moscow KLINICHESKAYA MEDITSINA in Russian Vol 68 No 10, Oct 90 pp 99-102 (Manuscript received 15 Mar 90)

[Article by Yu. N. Galkin, physician at the USSR Embassy in Denmark (Copenhagen); Y. O. Nilson, doctor of medicine, director, department of infectious diseases and AIDS at Vidovr Hospital (Copenhagen, Denmark); T. Erikssen, physician, department of infectious diseases and AIDS at Vidovr Hospital; and B. L. Bychenko, professor, doctor of medical sciences, regional advisor of the WHO European Regional Bureau (Copenhagen): "On the Clinical Classification of Acquired Immune Deficiency Syndrome"]

UDC 616.98:578.828.6]-092:612.017.1]-008.6

[Text] As we know, one of the most menacing diseases of the 20th century—HIV infection and its final stage, acquired immune deficiency syndrome (AIDS)—have assumed the nature of a real pandemic that has enveloped almost all countries of the world and has affected many spheres of human vital activities—social, economic, political, etc. In light of the extremely polymorphic nature of the clinical picture of the disease, many authors are trying to develop a general model of its basic clinical signs, which would make it possible to avoid the terrible consequences of both hyperdiagnosis and undetected cases of AIDS (as occurred, for example, with the first Soviet patient, Olga G., who died of AIDS in 1988).

In 1985, Haverkos et al.[3] proposed a system for the clinical classification of AIDS that divided patients into seven groups, according to the severity of their condition. Group 1 contained patients with an asymptomatic disease course, while group 7 contained patients with "full-blown" AIDS. In that same year, Blattner et al.[1] proposed a similar classification. Later, various classifications of the symptoms of HIV infection were developed.[3] In 1986, the American Centers for Disease Control (CDC, Atlanta, United States) proposed a variation of the classification.[6] It was based on dividing HIV-infected individuals into four groups, according to the stage of the disease's development and presence (or absence) of specific signs and symptoms—from acute HIV infection to various secondary diseases brought about by the action of the virus upon the human body. However, the proposed classification turned out to be highly arbitrary, and it did not become widely used, because of its many flaws.

In another classification that has been employed since 1987 at the recommendation of the CDC and was revised by WHO[2], all AIDS patients were divided into three groups: (1) individuals in whom laboratory tests for the virus have not been conducted; (2) individuals in whom the disease diagnosis is confirmed by laboratory data; (3) individuals who test negative for AIDS (for presence of the virus). That classification took into account the presence in the individuals of any of 11

so-called indicator diseases that are considered to be rather reliable criteria of AIDS, including six related to diseases typical of AIDS.[4] The classification widened the boundaries of the definition of AIDS by including in that concept, for the first time, severe and even fatal syndromes such as encephalopathy and the "emaciation syndrome", which afflict a considerable number of HIV-infected individuals; that doubtlessly helped increase the number of recorded cases of disease. However, that classification is not free of substantial flaws. Specifically, as with previous classifications, it fails to take into account certain acute and asymptomatic illnesses, for example, cases of persistent generalized lymphadenopathy in which diseases belonging to the AIDS "indicator" group are absent, and constitutional and neurological diseases that are less severe than HIV-induced encephalopathy and the emaciation syndrome. It should also be noted that the criteria for HIV-related encephalopathy and the emaciation syndrome are very complex, and there is some doubt as to whether those criteria were taken into account in all reported cases. Moreover, according to that classification, diseases serving as AIDS indicators must have a clear diagnosis, which is not always possible. Based on all that, the World Health Organization in 1987 developed and recommended a new classification of the clinical stages of AIDS, presented below in Table 1 (the classification was last revised in July 1989).

Table 1. Clinical Stages of AIDS[4]

Stage	Points
I. Asymptomatic	1
A. Persistent generalized lymphadenopathy	
II. Early signs of disease (at least one)	2
A. A weight loss of less than 10%	
B. Minor changes of skin and mucous membranes	
1. Seborrheic dermatitis	
2. Folliculitis	
3. Pruritis	
4. Psoriasis	
5. Fungal infection of the nails	
6. Recurrent ulcers in the mouth cavity	
a) Angular cheilosis	
7. Necrotic gingivitis	
C. Shingles for 5 years (in persons under 50)	
D. Recurrent upper respiratory tract infections	
III. "Intermediate" signs (at least one; i.e., the stage of "full-blown" disease)	3
1. Progressive weight loss (more than 10%)	
2. Diarrhea of unclear origin (for more than 1 month)	
3. Oral candidiasis	
4. Leukoplakia	
5. Pulmonary tuberculosis (in the recent past)	
6. Peripheral neuropathy	
7. Localized form of Kaposi's sarcoma	
8. Disseminated shingles	
9. Severe recurrent bacterial infections (pneumonia, pyomyositis, bacterial sinusitis)	
IV. Late signs of disease (at least one)	4
1. Pneumonia evoked by *Pneumocystis carinii*	
2. Toxoplasmosis	
3. Cryptococcosis	
4. Isosporosis	
5. Strongyloidiasis	
6. Cytomegalovirus infection	
7. Herpes simplex	
8. Progressive multifocal leukoencephalopathy	
9. Histoplasmosis	
10. Esophageal candidiasis	
11. Atypical mycobacteriosis	
12. Salmonellar septicemia	
13. Extrapulmonary tuberculosis	
14. Lymphoma	
15. Disseminated Kaposi's sarcoma	
16. Cachexia	
17. HIV-induced encephalopathy (disturbances of the central nervous system, dementia)	

It should be noted, however, that that classification is not very well suited for use in many developing (primarily African) countries, where laboratory capabilities are quite limited, which makes it impossible to establish the accurate diagnosis of opportunistic infection or tumors that the classification requires. Moreover, clinical manifestations of AIDS in developing countries differ considerably from those described in North America and Europe. In addition, in the opinion of a number of authors,[7] there are other flaws in the classification, including the following: (1) the absence of early nonspecific manifestations of HIV infection, as a result of which some cases of disease remain undiagnosed; and (2) the possible presence of not one, but several signs of disease in the individual, which, however, does not influence the prognosis (according to the classification).

Although we agree with the remarks presented above, we would like to express some of our own thoughts about certain items of the classification that appear rather debatable to us. From our point of view, the following may be named among the shortcomings of the classification:

1. No mention is made of pronounced weakness as one of the main signs of the disease. The same is also true for fever and night sweats.

2. The correctness of introducing diseases such as seborrheic dermatitis, folliculitis, pruritis, psoriasis, etc. (stage II, items B 1 - 4), into the classification as diagnostic criteria of AIDS is doubtful, since it unquestionably leads to hyperdiagnosis.

3. Many things are unclear in the description of stage IV of the disease. In particular, calling strongyloidiasis, herpes simplex, and extrapulmonary tuberculosis signs of the late stage of AIDS seems a mistake to us. In general, that system of pathology grouping is a clinical system rather than a laboratory system. For example, it makes a clinical distinction between "progressive multifocal leukoencephalopathy" (stage IV, item 8) and "HIV-induced encephalopathy" (stage IV, item 17). The former is more of an anatomical concept, whereas the latter is functional—i.e., what we have here are two hard-to-compare diagnoses.

4. There is no logic, completeness, or concreteness to the proposed classification; it is often unclear as to what the AIDS diagnosis is based on. For example, section IV, item 1, includes pneumonia induced by *Pneumocystis carinii,* which, as we know, is a frequent marker of AIDS in adults. But the authors of the classification give it four points, just as they do strongyloidiasis and herpes, for example.

5. "Recurrent upper respiratory tract infection" is placed in stage II D, as one of the possible early signs of AIDS; whereas "severe recurrent bacterial infection (pneumonia, etc.)" is placed in stage III, item 9. Here again, the grounds for the distinction are unclear. How and by what criteria is the severity of the individual's state assessed? That is, after all, quite a variable characteristic.

6. Pyomyositis and bacterial sinusitis are named among other signs of disease in stage III, item 9. As we know, pyomyositis is a rather rare disease, while bacterial sinusitis is an extremely nonspecific marker for AIDS, since it is encountered rather often in persons not infected with HIV.

7. The expression "Pulmonary tuberculosis in the recent past" (stage III, item 5) requires explanation. What does "in the recent past" mean? Why not in the present?

8. In our opinion, the expression "minor changes of the skin and mucous membranes" (stage II B) requires clarification. What signifies "minor"? Should pruritis (itching), which causes hardly any skin reaction, be placed in the same section with profound tissue alterations such as psoriasis, mycosis, and especially necrotic gingivitis?

9. On the whole, the proposed division of signs of disease into "early" and "late" appears unconvincing, indistinct and inconsistent to us, and the classification itself seems cumbersome and too detailed.

Recently, WHO proposed a simplified system, presented below (Table 2), for using a point count to identify individuals with AIDS.[7]

Table 2. System for Identifying AIDS by Point Count (WHO, 1988)

Disease Symptom	Points
1. Persistent generalized lymphadenopathy	0
2. (a) Changes in skin and mucous membranes	1
2. (b) Weight loss	1
2. (c) Pronounced fatiguability	1
3. Viral infection (herpes simplex)	2
4. Diarrhea lasting longer than 1 month	4
5. Fever lasting longer than 1 month	4
6. More than 10% weight loss for longer than 1 month	4
7. Pulmonary tuberculosis	5
8. Recurrent bacterial infections	5
9. (a) Leukoplakia	5
9. (b) Stomatitis, oral thrush	5
10. Delimited Kaposi's sarcoma	8
11. Cachexia	12
12. HIV-induced encephalopathy	12
13. Lymphoma	12
14. Opportunistic infections	12

According to that system, when the point count is 0 - 3, the probability of AIDS is low; at 4 - 11, AIDS is more probable; and at 12 points or more, AIDS is highly probable.

We feel that, despite its outward simplicity, the system also has a number of flaws.

1. The role that persistent generalized lymphadenopathy plays in this pathology is known. We cannot, therefore, understand why the system's authors attach so little significance to that symptom (0 points).

2. "Herpes simplex" is mentioned in item 3, but does herpes zoster really have less significance here?

3. It is unclear as to why varying degrees of weight loss are indicated as a specific sign of this pathology three times in the system (items 2b, 6 and 11), and with a 12-point difference in significance at that.

4. Item 2a, which covers too wide a range of pathology, is nonspecific.

5. The diagnosis presented in item 10 ("delimited Kaposi's sarcoma") actually precludes the possibility of acknowledging the generalized form of that disease, which is no less of an important "indicator" of AIDS.

6. Item 12 refers to HIV-induced encephalopathy. But if an individual is identified as an HIV carrier, use of the system for diagnostic purposes loses its meaning.

Thus, the system described above also needs improvement.

Noteworthy, from our point of view, is a clinical classification approved by the WHO in 1985,[4] according to which every case of AIDS in an adult must have at least two so-called major signs of disease and at least one "minor" sign in the absence of any known causes of immune suppression—causes, for example, such as cancer or extremely poor nutrition. According to that classification, the three "major" signs are constitutional: (1) loss of more than 10 percent of initial weight; (2) diarrhea lasting longer than one month; (3) prolonged fever (longer than one month), constant or intermittent. The six "minor" signs include the following: (1) persistent cough lasting one month or longer; (2) generalized pruritic dermatitis; (3) recurrent herpes zoster; (4) nasopharyngeal candidiasis; (5) chronic progressive disseminated infection evoked by herpes simplex virus; (6) generalized lymphadenopathy.

In order to study the feasibility of using that classification in the clinic, we examined a group of patients at the specialized AIDS treatment hospital (Vidovr). The patients had been diagnosed as having AIDS and were undergoing in-patient treatment from April 1988 to September 1989. Nineteen patients in whom the disease diagnosis had been confirmed when HIV was found in the blood were examined. Medical histories were obtained by interviewing the patients, while direct-observation data were obtained by examination. Table 3 presents some data obtained as a result of the survey.

Table 3. Main Symptoms of Disease in 19 Patients Infected With HIV (and diagnosed as having AIDS)

Disease Symptom	Number of Patients		Rank
	Absolute	% of Total Number of Patients	
1. Substantial weight loss (more than 10%)	12	63	4
2. Chronic diarrhea lasting longer than 1 month	3	16	6
3. Prolonged fever lasting longer than 1 month	18	95	1
4. Pronounced general weakness	18	95	1
5. Night sweats	14	74	2
6. Persistent cough lasting longer than 1 month	14	74	2
7. Generalized pruritic dermatitis	1	5	8
8. Recurrent herpes zoster	2	10	7
9. Nasopharyngeal candidiasis	10	53	5
10. Chronic progressive disseminated infection induced by herpes simplex virus	0	0	-
11. Generalized lymphadenopathy	13	68	3

Unlike the authors of that classication,[4] we do not consider generalized pruritic dermatitis, herpes simplex, or herpes zoster to be convincing, frequent signs ("markers") of HIV infection; that is also confirmed by the results of the survey: dermatitis was observed in only one of the 19 patients (i.e., in less than 5 percent of the cases); herpes zoster infection was observed in two (around 10 percent); and herpes simplex virus infection was not found in any of the subjects. Nor did we observe very frequent cases of diarrhea among European patients (four cases—20 percent of the subjects). However, we still feel it justified to include the term "chronic diarrhea" in that classification, especially in developing countries.

Thus, according to our data, the clinical specialist can propose AIDS if there is a lengthy course (at least one month) of a combination of three or more of the indicated symptoms: a feverish state, extreme weakness, pronounced sweating (especially at night), substantial weight loss, generalized lymphadenopathy, nasopharyngeal candidiasis, prolonged cough, or chronic diarrhea with no "visible" causes.

Conclusion

The AIDS classifications proposed to date (by WHO, CDC, etc.) have been intended to facilitate identification of the disease by practicing physicians on the basis of clinical symptoms. Those classifications were created when laboratory techniques for detecting the virus or antibodies to it were still under development. Accurate diagnosis of HIV infection became possible with the advent of those techniques. Detection of HIV in the body is evidence that the individual is in one of the phases of the disease. Therefore, when HIV infection is confirmed in the laboratory, any classification based on clinical symptoms and pursuing diagnostic goals loses its significance, though in some cases it might retain prognostic value.

In light of the above, despite having certain positive aspects, the classifications of HIV infection and AIDS that have been recommended by WHO, the CDC, and others for diagnostic purposes are not, in our opinion, suitable for use in the clinic. Those classifications are not specific enough, they are cumbersome and difficult to use in the absence of a laboratory service. On the basis of the experience of various researchers and on the basis of

our data (19 AIDS patients), we would like to propose a complex of symptoms (a system) that could be used to identify HIV-infected adults (aged 16 - 60).

The complex of symptoms manifested in adults infected with HIV includes the following:

I. Prolonged (longer than one month) presence of two or more of the listed symptoms

1. Unexplainable progressive weight loss (weight loss of more than 10 percent)

2. Feverish state of unclear origin, with temperature elevated to 38°C or higher

3. Heavy, previously unnoted sweating, especially at night

4. Persistent cough of unclear origin

5. Diarrhea of unknown origin

6. Considerable, previously unnoted general weakness, rapid tiring

II. Presence of at least one of the following factors in the medical history

1. Classification in one of the "risk groups":

a. Homosexuals, prostitutes

b. Drug addicts administering drugs with syringes

c. Persons given frequent blood tranfusions

d. Hemophiliacs

2. Sexually transmitted diseases

3. Recurrent infections

4. Neoplasms

5. Time spent abroad in regions endemic for AIDS

III. Presence of at least one of the following pathological signs identified revealed by direct-observation examination

1. Changes in skin and mucous membranes (herpetic rash, leukoplakia, mycosis, papillomas, etc.)

2. Polyadenopathy, lymphoma

3. Candidiasis

4. Recurrent pneumonia, pulmonary tuberculosis

5. Encephalopathy (in individuals under 50)

6. Kaposi's sarcoma

It should be noted that all of the 19 AIDS patients discussed above had some of the signs listed in that system. In our opinion, the system is sufficiently simple and convenient for examining an individual upon his first visit for medical assistance. Presence of two or more of the listed complaints, of one or more of the anamnestic factors, or of one or more of the signs detected by medical examination (see the chart) serves as grounds for further examination and observation of the patient, with mandatory elimination of the possibility of HIV infection by laboratory tests.

The system is offered here for clinical verification on a large number of patients in order to assess its specificity and sensitivity.

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Cholera in Moscow

91WE0093X Moscow TRUD in Russian 1 Nov 90 p 1

[Article by V. Ilin: "Cholera in Moscow: Round Two"; first paragraph is source introduction]

[Text] For the second time in two weeks, an individual with cholera arrived in the capital from abroad. Last time, the dangerous "guest" was brought in from India; this time, from Iraq.

On 28 October, Soviet citizen B. R-v flew in from Baghdad on Flight 514 and went directly to the medical station at Sheremetyevo Airport No 2. From there, he was transferred to Botkinskaya Hospital with a diagnosis of food poisoning. Tests yesterday, however, revealed cholera vibrio. The patient was immediately transferred to the infectious hospital on Sokolinaya Hill, and the department of especially dangerous infections of the city epidemiological station once again found itself with a

tough job—identifying the patient's contacts in the airplane, the airport, and Botkinskaya Hospital, and placing dozens of people under observation.

Aren't epidemic specialists having to be alerted a little too often? Unfortunately, there's nothing anybody can do about it—the range of contacts of our people with foreigners is widening swiftly. And the only thing that can be done in this regard is to reinforce and improve the epidemiological service, whose job is clear—to be our biological shield.

Preliminary Diagnosis of Plague in Moscow

91WE0093Y Moscow TRUD in Russian 14 Nov 90 p 1

[Article by A. Trushin: "Preliminary Diagnosis—The Plague"; first paragraph is source introduction]

[Text] Concern over several cholera cases (TRUD, 23 October 1990) had barely died down in the capital when the editor's office received another alarming report.

An extremely disheveled citizen was delivered by ambulance to City Hospital No. 1 directly from Kazanskiy Station at 1640 hours on 11 November. Because he had no documents with him, the doctors had to take him at his word. The vagrant gave his name as G. Kudryashev.

At 1930 hours on 12 November, Kudryashev passed away in the hospital's resuscitation ward. Plague was the preliminary diagnosis. We were told by the city epidemiological station that special epidemic-control measures are being conducted in Kazanskiy Station by a team from the epidemiological station of the Moscow Railroad, and people who had come in contact with the deceased are being identified.

Gennadiy Onishchenko, deputy chief of the Main Epidemiological Administration of the USSR Ministry of Health, said that the doctors had not yet come to a final conclusion concerning the patient's cause of death. Yesterday, an autopsy was done and tests were conducted. The management of City Hospital No. 1 assured us that Kudryashev had not come in contact with any other patients in the reception room or the resuscitation ward. Other details will become known in two or three days. We will report them to our readers.

Diphtheria Epidemic in Moscow

91WE0093Z Moscow VECHERNYAYA MOSKVA in Russian 9 Oct 90 p 1

[Article under the rubric, "Around the Capital: From 1 PM to 1 PM": "The Epidemic Has Not Been Conquered"]

[Text] Although we have begun talking less about diphtheria, and the frightening warnings have disappeared from the pages of the newspapers, it still cannot be said that the epidemiological situation in the capital has improved very much. The Studinformo Agency reports that to date, according to information provided by the city's epidemiological station, 376 persons have fallen ill since the beginning of the epidemic. Of them, 128 were in the "risk group"—i.e., persons in "contact" occupations—with 16 percent having the severe form of the disease. Unfortunately, 14 cases have been fatal (including three children). At present, 143,000 persons have been immunized. Immunizations are to be given to 300,000 - 400,000 persons by 1 November.

Plasmid Vector With Cascade Regulation of Expression of Genes

917C0048A Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 313 No 4, Aug 90 pp 980-982

[Article by M. A. Kamaletdinova, Sh. Z. Sagitov, R. R. Nabiullina et al.; Institute of Biology, Bashkir Scientific Center; Uralsk Department; USSR Academy of Sciences; Ufa: Institute of Cytology and Genetics; Siberian Department of USSR Academy of Sciences; Novosibirsk]

UDC 577.218+579.252.5

[Abstract] There is great interest in construction of vectors with indirect (cascade) regulation of expression of a built-in gene. In this case, synthesis of the regulator protein is controlled by an induced promotor, which controls the activity of the other cistron, regulating, in its turn, expression of the required gene. Construction of two types of vectors was described. The first type carries tandemly situated promoters P_R, P_L and the gene of the thermolabile repressor cI of phage λ. This vector is intended for direct induction of transcription of the built-in gene. The second type of vector is a derivative of the first and carries the gene of protein of the repressor of lac-operon under control of promotors P_R-P_L. This vector permits direct (cascade) induction of genes controlled by lac-promoter. The vectors obtained could be used for direct (pCP2) or indirect (pCi19) induction of expression of cloned genes. All of these vectors carry a tandem of potent promoters P_R and P_L of phage λ, the work of which is regulated by the thermosensitive repressor cI_{857}. Diagrams of construction of plasmids pCP2 and pCi19 were presented and discussed. The convenience of the system of regulation of activity of these genes lies in the fact that this makes it possible to unify control of different promotor-operator blocks, cloning genes of other protein-repressors in the same manner. Transcription of the gene required in this system is induced by reduction of the temperature of incubation of the medium but not by its increase. Figure 1; references 15: 7 Russian, 8 Western.

Immunomodulating Mechanism for Antitumor Activity of Asterin

917C0044E Moscow ANTIBIOTIKI I KHIMIOTERAPIYA in Russian Vol 35 No 6, Jun 90 (manuscript received 25 Jul 89) pp 31-34

[Article by V. V. Smirnov, Ye. L. Mishenkova, Yu. A. Grinevich, G. T. Petrenko, and S. V. Martynenko, Institute of Microbiology and Virology imeni D. K. Zabolotniy, UkSSR Ministry of Sciences; Kiev Scientific Research Radiology and Oncology Institute]

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[Abstract] The thymus-inductor activity of asterin was studied in 200 mice with Lewis carcinoma. Asterin was isolated from plants of the Asteraceae family by A. S. Bondarenko in the Institute of Microbiology and Virology imeni D. K. Zabolotniy of the UkSSR Academy of Sciences. Asterin is a complex of monoterpenes, sesquiterpenes, aromatic carbohydrates and oxygen-containing substances. The dose-dependent inhibition of proliferation in transplanted 3LL tumor cells observed with asterin, as well as several complete regressions of the neoplasm, demonstrated the anticancer activity of asterin. Administration of 50 mg/kg or 100 mg/kg asterin perorally four times a week for three weeks led to a statistically significant decrease in metastases. Number of metastases was reduced by 46 percent or 58 percent and average volume by 58 percent or 70 percent, depending on the dose. The antimetastatic effect observed was greater than the antitumor effect on the primary tumor. Asterin almost completely reduced the thymus index, indicating that it modifies the nonspecific morphological changes elicited by malignant invasion. The thymus serum factor level reduction induced by the neoplasms was partially restored by the asterin treatment in both latent and terminal periods. This effect reached a maximum 30 days after tumor transplantation. These results confirm the hypothesis that the mechanism of asterin activity is connected with activation of immune reactions in T-cell immunity. Both direct effects on tumor cells and indirect effect on the protective functions of the organism are involved in the mechanism of asterin action. Figures 2; references 18: 13 Russian, 5 Western.

Efficacy of Myelopid in Immunodeficiency

917C0214B Moscow TERAPEVTICHESKIY ARKHIV in Russian Vol 62 No 12, Dec 90 (manuscript received 12 Sep 89) pp 81-87

[Article by R. V. Petrov, A. M. Borisova, A. V. Glazko, A. V. Simonova and R. N. Stepanenko, Institute of Immunology, USSR Ministry of Health, Moscow]

UDC 053.8-092:612.017.1]-085.36183-036.8-07

[Abstract] Double blind therapeutic studies were conducted on 220 immunodeficient subjects to assess the efficacy of myelopid in chronic pneumonia, agammaglobulinemia and selective IgA agammaglobulinemia. Myelopid (B-activin) consists of a complex of heat-stable 500 - 3000 D peptides that was first isolated from bone marrow at the Institute of Immunology and shown to modulate B cell immunity. The experimental patients were treated subcutaneously with 6 mg every other day for three days, with the entire course reated twice after 10 days. Monitoring of the immune status of these patients showed myelopid led to prolonged remissions of ca. one year in 78 percent of the patients, whereas the incidence of remissions in control patients was 30 percent. In addition, remissions were also obtained in patients with agammaglobulinemia who otherwise failed to respond with remissions. Furthermore, myelopid was shown to be more effective in inducing remissions when administered during a phase of exacerbation, leading to longer remissions. The patients tolerated myelopid well, with only three reporting onset of short-term thirst 2 h after injection. Administration of myelopid favored an increase in T (especially helpers) and a 4-fold increase in B cells, and appearance of immunoglobulins (including IgA). Analogous results were obtained with treatment schemes consisting of 3 mg intravenously, 6 mg subcutaneously and 6 mg intravenously. Figures 9; tables 1; references 15: Russian.

Hygienic Aspects and Methodological Bases of Creation of Bioinert Polymer Materials With Prescribed Properties for Clothing and Equipment for Individual Protection

917C0075A Moscow GIGIYENA I SANITARIYA in Russian No 7, Jul 90 pp 9-13

[Article by G. P. Bogachuk and G. L. Mondoyev; Institute of Biophysics; USSR Ministry of Health; Moscow]

UDC 614.35:[615.46.03:614.89

[Abstract] The most important qualities of polymer materials to be used in protective clothing and devices include chemical stability, bioinertness and safety in use for humans under prescribed conditions of use. Creation of non-toxic, high-quality synthetic compositions require the combination of many contradictory properties in a single sample of polymer materials. Quality of a polymer is determined basically by three factors: compounding composition, supermolecular structure and external effects. A generalized function of desirability of properties was defined as the mean of geometrically particular desirabilities and was determined by a formula which permits maximum or optimum determination of desirability of properties of polymer materials. The general principles and sequence of studies for optimization of compositions and properties of polymers for a prescribed purpose were tabulated and discussed. Use of this system permitted the user to avoid repetition of previous studies and to study, on an electronic computer, all conceivable and inconceivable combinations of compounding factors, to choose the best, to give the required value to any particlar property, to bring a complex indicator of quality to an extremum while maintaining controllable properties at a fixed limit and to check the accuracy of prediction of calculated properties of optimal compositions with consideration of the unlimited number of requirements. Figures 2; references 5: Russian.

Effects of UV Laser on Corneal Endothelium

917C0229B Odessa OFTALMOLOGICHESKIY ZHURNAL in Russian No 3, 1990 (manuscript received 24 Nov 88) pp 173-175

[Article by L. A. Linnik, professor, L. I. Khmelik, senior scientific fellow, T. A. Krasnovid, cand. med. sci., and K. G. Drachenko, sen. sci. fellow, Odessa Order of the Red Banner of Labor Scientific Research Institute of Eye Diseases and Tissue Therapy imeni Academician V. P. Filatov]

UDC 617.713-018.7-085.849.19-092.9

[Abstract] In view of the expanding use of UV lasers in the management of keratitis, further analysis was conducted on its effects on corneal endothelium in rabbits. The experimental design involved irradiation of one eye of 2.5 - 3.5 chinchilla rabbits with high frequency nitrogen LGI-505 laser (5 - 20 mW/cm^2; 1 - 15 min, λ = 0.337 mm). Continuous monitoring of the corneal epithelium by means of contact mirror microscopy, beginning 1 h after irradiation and continuing for three months showed that the procedure was entirely safe with no changes in the endothelium. Figures 1; references 20: 12 Russian, 8 Western.

Local and Systemic Stimulant Effects of Helium-Neon Laser Eye Irradiation in Rabbits

917C0229C Odessa OFTALMOLOGICHESKIY ZHURNAL in Russian No 3, 90 (manuscript received 28 Feb 89) pp 176-178

[Article by V. V. Sokolovskiy and I. N. Ushkova, drs. med. sci., Yu. D. Berezin, L. A. Pokrovskaya, L. P. Rodionova and L. L. Goncharova, cands. biol. sci., N. Yu. Malkova, engineer, and I. N. Makarova, junior sci. fellow, Sanitary Hygienic Medical Institute; Scientific Research Institute of Labor Hygiene and Occupational Diseases, Leningrad]

UDC 617.7:615.831.8:612.085.2

[Abstract] An analysis was conducted on the local and systemic stimulant effects of LG-78 hemium-neon laser following eye irradiation in male chinchilla rabbits. The resultant findings showed that eye irradiation for 10 min/day for 10 days with a diffuse beam (λ = 0.63 mm; 30 mW/cm^2; 8 x 10E-6 W x cm^{-2} illumination) enhanced blood flow in the uveal tract after five days of treatment without any effects on systemic hemodynamics. After 10 days additional effects included elevated systolic (6.9 percent) and diastolic blood pressures (9.9 percent), and increases in minute volume (21.6 percent) and stroke volume (15.4 percent) in the absence of significant changes in the control of cardiac activity. Biochemical studies revealed activation of the antioxidant system in the blood and especially retina, particularly in the eye that was irradiated. References 16: 14 Russian, 2 Western.

Normalization of Protein Synthesis in Rat Brain Dystrophic Neurons After Hypoxia, Opening of the Hemato-Encephalic Barrier and Effect of Organ-Specific RNA

907C0843A Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 312 No 6, Jun 90 pp 1491-1494

[Article by L. V. Polezhayev, L. V. Cherkasova, V. N. Vitvitskiy and A. V. Timonin; Institute of General Genetics imeni N. I. Vavilov; USSR Academy of Sciences; Moscow]

UDC 591.089.84.612.8

[Abstract] The article described results of a study including an attempt to normalize dystrophic brain cell neurons, eliminating proliferation of slightly-differentiated brain cells by use of organ-specific RNA which stimulates development and regeneration of homologous organs and tissues; it is harmless and never causes malignancy. The study also includes an attempt to produce a normalizing effect without mechanical injury to the brain in order to prevent injury to the brain and formation of neurotropic factors. Large-molecular RNAs were injected into the thigh muscles of rats with undamaged hemato-encephalic barrier and rats under the effect of hypoxia in which the hemato-encephalic barrier was opened the day after the hypoxia session. The opening grew for seven days and then decreased and disappeared within 35 days. Rats (140 - 160 g) received intramuscular injections of 125 μ RNA 1, 3, 6 and 7 days after the hypoxia session. Intensity of incorporation of ^{3}leucine determined protein synthesis after decapitation of the rats eight and 130 days after the hypoxia session. Autoradiographic studies showed that hypoxia decreased protein synthesis in the early (eight days) and late (130 days) course of the experiment. Intramuscular injection of RNA after hypoxia increased protein synthesis in the early and late periods of the experiment, exceeding the initial protein levels in some series of experiments. RNA injection into intact rats lowered protein synthesis in the neurons in the early period but increased it to levels above the initial level in the late period. Biochemical studies confirmed these findings. The study demonstrated that it is possible, after opening the hemato-encephalic barrier and intramuscular injection of RNA isolated from cerebral nerve tissue, to stimulate and normalize reduced protein synthesis in cerebral neurons. This suggested the possibility of using such a method to normalize both the structure and function of cerebral brain tissue. Figures 2; references 14: 9 Russian, 5 Western.

Repeated Transplantation of Embryonal Nerve Tissue Into Brain of Mammals

907C0843B Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 312 No 6, Jun 90 pp 1495-1496

[Article by L. V. Cherkasova; Institute of General Genetics imeni Vavilov; USSR Academy of Sciences, Moscow]

UDC 591.089.84.612.8

[Abstract] Adult pubescent female Wistar rats (9) underwent hypoxic hypoxia and six surviving after one month underwent allotransplantation of fragments of cerebral cortex tissue from 15 16-day-old embryos of normal rats into the sensomotor cortex of the right hemisphere. After three months, the same rats underwent implantation of fragments of cortical tissue from 15 16-day-old embryos of normal rats into the sensomotor region of the left cerebral hemisphere. After three months, the rats were decapitated and brain sections were prepared. Six months after the first transplantation and three months after the second, the two transplants were seen in all experimental rats. Primary transplants grew vigorously, reached huge sizes, filling the entire ventricular cavity. Histological study of both the primary and secondary transplants showed that neurons of the transplants, gathered into a cluster, did not form layered cytoarchitectonics inherent to normal rats. Most of the neurons of the intraventricular or intraparenchymal transplants were differentiated. Many neurons were in a hypochromic or a hyperchromic state. Small vessels and capillaries appeared frequently in the intraventricular transplants. The number of dying and degenerating cells were much greater in the primary intraventricular transplants than in the secondary transplants. The study showed the possibility of repeated transplantation of embryonal nerve tissue into the brain of adult rats, subjected to hypoxic hypoxia. Both types of tranplants survived, grew, enlarged and did not disengage in the six months of the experiment. Neurons of neither transplant formed normal cytoarchitectonics. Figure 1; references 8: 3 Russian, 5 Western.

Use of Dalargin in Complex of Anesthesiological Protection During Surgery on Organs of Abdominal Cavity

917C0052A KHIRURGIYA in Russian No 7, Jul 90 pp 75-81

[Article by V. V. Likhvantser, B. M. Shloznikov, V. I. Smirnova et al.; Department of Anesthesiology and Reanimatology (acting director, candidate of medical sciences V. I. Smirnova); Biochemistry Laboratory (director-professor A. A. Karelin); Institute of Surgery A. V. Vishnevskiy (director-member of the USSR Academy of Sciences V. D. Fedorov), Moscow]

UDC 617.55-089.5:[615.31:547.95:547.943

[Abstract] Use of dalargin in multicomponent balanced anesthesia in abdominal surgery was tested on 36 patients undergoing abdominal organ surgery. A randomized group of patients undergoing neuroleptoanalgesia served as a control group. The use of dalargin greatly reduced (6-fold) the need for narcotic analgesics during the surgery without decreasing the effectivenss of anesthesia. Hepatoprotective properties of dalargin reduced the stress of the patient during surgery. Similar effects have been noticed during use of dalargin in lung

and open heart surgery. The decrease of total peripheral resistance and increase of elasticity of the arterial reservoir in patients receiving dalargin were attributed to the autonomic priming of dalargin. The study confirmed the advisability of using dalargin in multicomponent, balanced anesthesia. Figures 5; references 10: 7 Russian, 3 Western.

Use of Combutec 2 in Treatment of Patients With Radiation Injuries of Skin

917C0052B Moscow MEDITSINSKAYA RADIOLOGIYA in Russian Vol 35 No 7, Jul 90 pp 33-34

[Article by L. G. Selezneva, A. V. Barabanova, A. A. Adamyan et al.; Institute of Biophysics; USSR Ministry of Health; Moscow]

UDC 616.5-001.17-02:615.849]-085.468.295-036.8.07

[Abstract] Combutec 2 consists of cream-colored or dark cream-colored pads based on soluble collagen and differs from Combutec 1 in that it contains antiseptics: a boric acid solution or a dioxidine solution. Victims (26) of the Chernobyl Atomic Power Plant accident with vast burns from β-radiation burns against a background of acute radiation sickness with combined radiation-burn injuries received extensive infusion antibacteria therapy with the use of Combutec 2 pads. Effect of the use of Combutec 2 in different patients with different problems was described. Use of these pads confirmed their high therapeutic effectiveness in treatment of patients with radiation injuries. It can be used in all periods of development of skin radiation injuries. References 2: Russian.

Study of Hemocompatibility of New Hydrogel Sorbent in Endogeneous Intoxication Syndrome

917C0060A Dushanbe ZDRAVOOKHRANENIYE TADZHIKISTANA in Russian No 3, May-Jun 90 pp 43-46

[Article by B. M. Nurkhanov; Scientific Research Institute of Medical Radiology; USSR Academy of Medical Sciences]

[Abstract] A study of the effect of the hydrogel sorbent IKhANT on the state of the peripheral blood of dogs during the endogeneous intoxication syndrome paralleled a study of the effect of the most common carbon sorbents SKN-4M. The first series of experiments, begun 24 hours after the beginning of development of endogeneous intoxication syndrome, involved collection of 450 ml of blood from the vena cava of five dogs and passage of portions of blood through columns with equal volumes of hydrogel and SKN-4M. In the second series of experiments, within six hours from beginning of the development of endogeneous intoxication syndrome, one hemosorption session involved eight dogs receiving sorbent IKhANT and four receiving SKN-4M. Experiments in vitro involved a count of the number of erythrocytes, leukocytes and thrombocytes and determination of the hematocrit and hemoglobin level. In the first series of experiments, passing the blood through hydrogel hemosorbent IKhANT did not decrease the number of formed elements. The carbon sorbent in the system in vitro decreased the number of erythrocytes by 50 percent, the number of leukocytes by 54 percent and thrombocytes by 62 percent. The hemoglobin level and hematocrit number decreased. The second series of experiments showed that hemosorption with use of SKN-4M sorbent reduced the number of erythrocytes by 50 percent, the number of leukocytes by nearly 12 percent and the number of thrombocytes by 32 percent. The use of hydrogel sorbent for extracorporal detoxication of the body did not affect the quantitative composition of the peripheral blood of the dogs during modeling of the endogeneous intoxication syndrome. IKhANT has clear advantages over the sorbent SKN-4M. References 6: 5 Russian, 1 Western.

Biospecific Antiprotease Hemosorbent "Ovosorb" in Treatment of Experimental Peritonitis

917C0071A Minsk DOKLADY AKADEMII NAUK BSSR in Russian Vol 34 No 10, Oct 90 pp 951-954

[Article by V. V. Kirkovskiy, V. N. Gapanovich and G. A. Lobacheva, Minsk State Medical Institute]

UDC 616.381-002:615.246.2+615.38-015.2

[Abstract] A study of the possibility of correcting protein metabolism by the use of the biospecific antiprotease hemosorbent "Ovosorb" during experimental peritonitis involved experiments on 17 - 23 kg mongrel dogs on ordinary vivarium rations. Study of the dynamics of change of constants of protein metabolism in control and experimental groups of animals with experimental purulent peritonitis during complex treatment, without use of "Ovosorb" and with its use, showed the high effectiveness of the new generation of biospecific sorbents "Ovosorb" in correction of severe disturbances of protein metabolism and the endotoxicosis connected with it during experimental purulent peritonitis. Figures 2; references 13: 12 Russian, 1 Western.

Disturbances of Microcirculation in Kidneys of Animals After Acute Blood Loss, Acute Alcohol Intoxication, Acute Sepsis and Their Correction by LB-1

917C0071B Yerevan KROVOOBRASHCHENIYE in Russian Vol 23 No 3, May-Jun 90 pp 61-63

[A. A. Kagramanyan, G. Sh. Amiridze and T. G. Chigogidze; Scientific Research Institute of Urology and Nephrology, Ministry of Health, GSSR]

UDC 616.1:616.61

[Abstract] Study of the changes in the intensity of local blood flow in the kidneys in different pathological states involved polarographic determinination of the intensity of local blood flow in the surface layer of the cortical zone of the kidneys, in the cortical layer and in the medullary layer. The study included eight series of experiments on 80 Chinchilla rabbits weighing 1.4 - 2.5 kg. Blood drawn from the femoral artery equalled 18 percent of the total circulating blood. Injection of a 40 percent solution of ethyl alcohol once at the rate of 3.5 ml/kg of weight of the rabbit produced acute alcohol intoxication. Intraperitoneal injection of a microbrial emulsion of golden staphylococcus strain No. 4293 produced a model of acute sepsis. The biopreparation of the interferon series, LB-1, was administered in four series of experiments. Use of LB-1 increased local blood flow in all layers of the kidney. Total renal blood flow increased by 15 percent and intrarenal redistribution of blood flow did not occur. Use of LB-1 after acute blood loss increased blood flow in all layers of the kidney. In the group with acute alcohol intoxication, use of LB-1 increased local blood flow in all layers. Injection into rabbits with sepsis increased local blood flow in the surface layer of the cortical zone by 42 percent with practically no change of local blood flow in the cortical layer and medullary layer. The total renal blood flow increased by 10 percent in comparison with untreated rabbits with sepsis. Use of LB-1 clearly increased the total renal blood flow and corrected intrarenal redistribution of blood flow.

Study of Optical Properties of New Dressing Materials With Biologically Active Substances

917C0072A Yerevan ZHURNAL EKSPERIMENTALNOY I KLINICHESKOY MEDITSINY in Russian Vol 30 No 3, May-Jun 90 pp 220-223

[Article by M. T. Aleksandrov, A. V. Gertsen, B. N. Arutyunyan et al.; Scientific Research Institute of Laser Surgery, Ministry of Health, USSR]

UDC 615.46

[Abstract] A study of optical characteristics of dressing materials with biologically active substances which produce a pronounced effect at different stages of pathogenesis of a purulent wound in the dynamics of reparative regeneration was performed with use of a helium-neon laser device and a gallium-arsenide semiconductor radiator. Optical parameters of the materials were determined with use of active laser biophotometers. Knowledge of the values of optical density of the dressing materials may ensure individual determination of a stably reproduced dose of the effect of laser irradiation during combined medicamental laser therapy of surgical diseases. The results will promote further development of the use of helium-neon and infra-red laser irradiation in complex therapy of surgical diseases. Figure 1; references 4: Russian.

Problem Concerning Group Morbidity From Botulism Type "A"

917C0072B Yerevan ZHURNAL EKSPERIMENTALNOY I KLINICHESKOY MEDITSINY in Russian Vol 30 No 3, May-Jun 90 pp 240-244

[Article by V. D. Oganesyan, S. M. Agadzhanyan, V. M. Agadzhanyan and L. M. Mkhitaryan; Yerevan Institute for Advanced Training of Physicians; Yerevan Medical Institute]

UDC 616.981.553

[Abstract] A study of specific features of manifestation of the disease and the course of type A botulism patients ranging in age from 9 - 64 years was described and discussed. Botulism A followed consumption of salted chervil (32 cases), consumption of purslane (eight cases) or home-canned tomatoes (eight cases). All patients received polyvalent antibotulism serum with gradual reduction of dosage and number of doses in proportion to regression of neurological symptoms. Early allergic reactions in the form of urticaria and anaphylactic shock developed in three persons. Serum sickness occurred in five patients 8 - 11 days after serum injection. Other complications included pneumonia and myositis. In uncomplicated cases, all symptoms disappeared by day 10 - 16 after mild cases, on day 13 - 15 after cases of average severity and by day 20 - 36 after severe cases. Women prevailed in the structure of group morbidity of botulism "A". The clinic of type "A" botulism was distinguished by significant polymorphism with high frequency of signs of ophthalmoplegia, phagoplegia and myoplegia. The disease usually presented with disturbances of vision and swallowing. Signs of hyposalivation preceded other symptoms in 29 percent of the patients and the disease began with gastroenteritis in only 6 percent of the cases. Basic symptoms of type "A" botulism found in the group were tabulated and analyzed. References 5: 4 Russian, 1 Western.

Use of Helium-Neon Laser Beam During Toxemias in Pregnant Women, Parturients and Puerperants

917C0116 Minsk ZDRAVOOKHRANENIYE BELORUSSII in Russian No 9, Sep 90 pp 13-18

[Article by K. I. Malevich, P. S. Rusakevich and L. V. Vilenchik; 2nd Chair of Obstetrics and Gynecology (head-professor K. I. Malevich); Belorussian Institute For Advanced Training of Physicians]

UDC 618.2+618.4.+618.61-036.1:618.3-008.6:615.849.19

[Abstract] A detailed study of the clinical course of pregnancies and births complicated by toxemia and treated by He-Ne laser therapy and minimal doses of sedative, hypotensive, spasmolytic, antioxidant, disintoxication and other symptomatic drugs involved a study of 177 women with toxemia in the third trimester of pregnancy. The use of helium-neon laser therapy and minimum doses of other medications promoted rapid and persistent remission and produced earlier disappearance of basic clinical manifestations. The procedure greatly reduced complications of pregnancy and decreased the number of surgical interventions required. It shortened the rehabilitation period and ensured earlier release from the hospital. It prevented negative side effects for the mother and fetus. The method proved to be simple and superior to the traditional medication program because it decreased the effect of drugs for the mother and the fetus. Figure 1; references 6: Russian.

Management of Hypertensive Crisis With Dry Immersion Hydrotherapy

917C0214A Moscow TERAPEVTICHESKIY ARKHIV in Russian Vol 62 No 12, Dec 90 pp 44-47

[Article by S. G. Ivanov and L. I. Markova, Chair of Therapy, Moscow Medical Stomatological Institute imeni N. A. Semashko]

UDC 616.12-008.331.1-039.31-085.83-036.8-07

[Abstract] Therapeutic trials were conducted on the management of hypertensive crises with 90 min of dry immersion hydrotherapy in the case of 26 men (53 +/- 1.9 years) and women (55.5 +/- 1.7 years). The water bath was maintained at 33 - 35°C and the patients immersed at an angle of 35 - 40° to the thorax while swathed in impermeable cloth. The method was found effective in 85.8 percent of the patients with hypertension due to elevated peripheral vascular resistance and in 80 percent of those with increased cardiac output. Primary changes in the former cohort consisted of a 47.27 mm Hg fall in systolic blood pressure and a 17.9 mm Hg fall in diastolic pressure, and a 14.5 percent reduction in peripheral vascular resistance. In the latter group the predominant benefits were represented by 47.1 and 14 mm Hg reductions in systolic and diastolic pressures, respectively, and a 28.7 percent reduction in the stroke volume. In general, the dry immersion form of hydrotherapy had a calming effect on the patients and promoted diuresis and appears to be an attractive alternative to chemotherapy in hypertensive crises. Figures 1; tables 1; references 17: 13 Russian, 4 Western.

Hemosorption Therapy in Rheumatoid Arthritis

917C0227A Kiev VRACHEBNOYE DELO in Russian No 11, Nov 90 (manuscript received 11 Dec 89) pp 50-51

[Article by L..S. Kriklivets, S. M. Ginzburg, V. I. Maltsev, A. V. Medvedev, V. S. Didyk and Yu. K. Kriklivets, Zhitomir Oblast Hospital]

UDC 616.15-02:616.61-078:616.72-002.77

[Abstract] Therapeutic trials were conducted on 30 male and female patients, 25 - 50 years old, with rheumatoid arthritis. Seven days after therapy the status of 28 patients showed objective clinical improvement in terms of attenuation of joint inflammation and reduction of morning stiffness. In addition, clinical chemistries demonstrated a marked reduction in the ESR from 34 to 17 mm/h, as well as a reduction in IgG from 24 to 18 percent. The final clinical impression was that hemosorption was most effective in younger patients (< 30 years) still in the initial stages of rheumatoid arthritis. Tables 1; references 6: Russian.

Clinical, Diagnostic and Therapeutic Aspects of Craniothoracic Trauma in Relation to Age

917C0247A Kiev KLINICHESKAYA KHIRURGIA in Russian No 10 Oct 90 (manuscript received 18 Oct 89) pp 1-3

[Article by G. A. Pedachenko, Ye. G. Pedachenko and Yu. V. Smalyukh, Kiev Scientific Research Institute of Neurosurgery, Ukrainian SSR Ministry of Health]

UDC 617.51+617.54]-001-053-07-089

[Abstract] A comparative analysis was conducted on the outcome of 125 cases of combined brain and chest injuries with 53 cases of brain injury. The clinical impression was that in combined cases symptoms attributed to brain injury overshadow symptomatology due to chest trauma leading to significant diagnosic errors. The majority of such errors occurred in patients with severe brain and chest damage or severe brain damage in combination with nonthreatening chest injuries. In 44 percent of such cases chest injuries were not recognized initially and in 21.6 percent brain injuries were overlooked. In all cases of craniothoracic trauma, regardless of age, the prognosis was guarded because combined respiratory and hemodynamic distress had a mortality rate approaching 96 percent. The clinical evaluations showed that primary diagnostic efforts should be directed at identifying craniocerebral trauma, chest injuries, and secondary manifestations of brain injury requiring immediate surgical intervention. Such information is best acquired via head and chest x-rays, echoencephalography, CAT scans, and carotid angiography. Subsequent diagnostic strategy should concentrate

on sequelae of brain injuries, such as cerebral edema and secondary hemodynamic disturbances. References 1: Russian.

Clinical Aspects of Thoracoabdominal Trauma Superimposed on Brain Injury

917C0247B Kiev KLINICHESKAYA KHIRURGIA in Russian No 10 Oct 90 (manuscript received 2 Oct 89) pp 4-6

[Article by A. P. Korol, V. F. Michurin, A. K. Zeltser and S. V. Konovalov, Chair of Anesthesiology and Resuscitation with a Neurosurgery Course, Odessa Medical Institute imeni N. I. Pirogov]

UDC 617.54/55-001-089:618.831-001

[Abstract] Clinical assesment was conducted on 31 cases in which thoracoabdominal injuries were superimposed on brain injuries. Seven of the patients died. The analysis showed that primary therapeutic efforts should be directed at controlling hemorrhage, shock, and restoring functional potential of affected organs. In light forms of brain injury primary efforts were directed at management of thoracic and abdominal organ pathology and their sequelae. In cases of severe brain damage in combination with serious trauma of chest and abdominal organs and ongoing hemorrhage into the chest or peritoneal cavities; control of hemorrhage should take precedence over brain surgery. In the absence of hemorrhage in the chest and/or abdominal cavities, the immediate surgical intervention should be on the brain, followed by thoracic and abdominal surgery in conjunction with rehydration and antihypoxic therapy. In addition, patients in shock were best treated by means that did not involve physical insult. Finally, as a rule older patients required 15 - 30 days more of hospitalization than did the younger cohort.

Effects of Postoperative Hemosorption on Pulmonary Function in Acute Ileus

917C0247C Kiev KLINICHESKAYA KHIRURGIA in Russian No 10 Oct 90 (manuscript received 7 Dec 89) pp 40-44

[Article by V. G. Ryabtsev, B. S. Myslovatyy, Yu. B. Kutsyk, M. Ya. Aliyev, F. D. Dzheyranov and S. A. Deputovich, Chair of Surgerical Diseases, Sanitary Hygienic Faculty, 1st Moscow Medical Institute imeni I. M. Sechenov, Moscow]

UDC 616.34-007.272-089:615.246.0-06

[Abstract] An analysis was conducted on the efficacy of postoperative hemoperfuson (HP) through an adsorbent column (hemosorption) in 55 cases of acute ileus. The patient cohort was represented by men and women, 60 percent of whom were older than 60 years. Depending on their clinical state, 1 - 4 veno-venous HPs were performed (ADB, FAS, SKN-4, or SKN-1 adsorbents; 40 - 150 ml/min flowrates for 40 - 100 min, equivalent to 1 - 1.5 x circulating blood volume). The immediate benefits of HP consisted of a 65 percent reduction in plasma toxicity in the paramecium test, and a 17 - 23 percent reduction in intermdiate MW molecules. However, both P_vO_2(tab)and P_aO_2 were reduced by 8 mm Hg after HP, values which did not recover to baseline after 24 h of monitoring. Accordingly, positive pressure ventilation was employed in 20 patients with multiple HPs which led to an increase in P_vO_2 and P_aO_2 by 8 mmg Hg in ca. 12 h with attendant clinical improvement in respiratory performance. Accordingly, HP has been shown to be an effective modality in controlling endogenous intoxication in patients with acute ileus, and its hypoxic sequelae can be effective when controlled by positive pressure breating.

Contemporary Problems in the Vaccinal Prevention of Infectious Diseases and Approaches to Solving Them

917C0311A Moscow TERAPEVTICHESKIY ARKHIV in Russian Vol 62 No 11, Nov 90 (manuscript received 27 Jun 90) pp 3-7

[Article by V. I. Pokrovskiy, S. K. Litvinov, and V. M. Bolotovskiy; Central Scientific Research Institute [TsNII] of Epidemiology, USSR Ministry of Health [Minzdrav SSSR], Moscow]

UDC 616.9-085.371

[Text] The vaccinal prevention of infectious diseases is a highly effective measure of influencing the epidemic process of these diseases. The system of planned immunization of the population which has been developed by our scientists and the many years of its existence have demonstrated the undoubted effectiveness of this method of combating such infectious diseases as diphtheria, whooping cough, tetanus, measles, poliomyelitis, etc. Moreover, the widespread and goal-directed use of vaccinal prevention of smallpox has led to the elimination of this infection in our country. The experience accumulated has made it possible for Soviet scientists (L. A. Favorova, V. A. Bashenin, L. V. Gromashevskii, V. M. Zhdanov, and others) to develop scientifically substantiated approaches to the elimination of infectious diseases [1, 3, 4, 7] which have been widely used by the WHO in the campaign against smallpox. This ended its existence in the world in 1977, when its last case was recorded in Somalia.

Significant advances in the reduction of morbidity from diphtheria and tetanus in the countries of Europe, the United States, Canada, etc., have been achieved as a result of the introduction of planned immunization. The incidents of pertussis in the countries of Eastern Europe, France and the United States has decreased significantly.

The sharp decrease in the incidence of paralytic poliomyelitis in Europe, where it had reached a level of 0.01 per 100,000, is associated with the use of live poliomyelitis vaccine. Significant successes have been noted in the reduction of morbidity and mortality from measles in the Scandinavian countries, France, Hungary, Bulgaria, Japan, Canada, and the United States, while in Czechoslovakia measles has been practically eradicated [11].

According to the data of the USSR Ministry of Health, vaccinal prevention has led in our country to a decrease in the incidence of diphtheria by a factor of 85.5, of poliomyelitis by a factor of 111.7, of measles by a factor of 53.6, and of pertussis by a factor of 19.7, as compared with the prevaccine period; mortality from these infections has also decreased. On the other hand, the rate of reduction in morbidity has significantly slowed in the last 7 - 8 years, and with respect to some infections it has even increased. Thus, according to our data, the incidence of poliomyelitis remained at the level of 0.06 per 100,000 from 1980 through 1987, and the incidence of measles decreased from 133.9 to 67.7 per 100,000, although it remained at the previous level in the RSFSR, the Georgian, Kazakh, and Tadzhik SSR, and in the Turkmen, Armenian, and Lithuanian SSR it was even observed to increase. An increase in the incidence of pertussis from 5.2 in 1980 to 7.1 per 100,000 in 1987, and diphtheria from 0.13 to 0.38 per 100,000 was observed in the same time period. This is associated with the fact that insufficient attention has been devoted in recent years in this country to the solving of the problems of vaccinal prevention of the infectious diseases, and to the fact that comprehensive measures to improve vaccination operations have not been carried out. As a result of certain shortcomings in this work, the coverage of the child population with inoculations has proven to be extremely low. According to our data, children up to the age of one year who have been vaccinated against diphtheria and pertussis in the Moldavian SSR in 1988 was only 33.6 percent; poliomyelitis, 35.5 percent; in the RSFSR, 34.2 and 35.3 percent; in the Estonian SSR, 26.9 and 27 percent, and in the Belorussian SSR, 38.5 and 38.7 percent, respectively. Overall, this indicator has remained very low throughout the country as well, 38.6 and 40.8 percent, respectively. At the same time, theoretical developments, as well as Soviet and foreign practical experience with vaccination operations indicate that stable and distinct results cannot be expected without covering the susceptible population with inoculations in 90 - 95 percent of cases. However, in accordance with the practice accepted by the USSR MInistry of Health, the official statistical data provide a notion of the extent of inoculation within the country only once in four years, which naturally does not permit following vaccination operations on an expeditious basis, nor the introduction of the necessary adjustments. Moreover, these data create the impression of a totally favorable situation. From our point of view, it is necessary to introduce into public health practice the collection of data regarding the coverage of children up to the age of one year with inoculations, when each child should have received BCG, three inoculations with DPT vaccine, and three with poliomyelitis vaccine. This would permit the assessment of the effectiveness of vaccination operations. The age of 12 months is the advisable age for inoculation against measles in our country; it is probably advisable, in addition, to analyze the data on the inoculation coverage for this group of children up to two years of age.

The level of coverage of children with inoculations depends directly on the amount of medical allocations for the various inoculations. Unfortunately, the amount of these allocations, according to the WHO data, is already rather high in a large number of countries; and the USSR does not constitute an exception. Thus, the percentage of children up to one year of age not vaccinated against diphtheria was 34.3 in 1982 in the RSFSR, 30.5 in the Belorussian SSR, and 50 in the Moldavian SSR. The percentage of those not inoculated against poliomyelitis in the same republics was 30.6, 30.2, and 31.7, respectively; in the Estonian SSR, 50.2, and in the Latvian SSR, 23.8. Children up to age two not inoculated that year against measles was 36.7 percent in the RSFSR and 58.2 percent in the Estonian SSR. The percentage of provisional medical allocations varies a great deal. Thus, in the case of measles vaccinations, it was 10.6 in 1982 in the Estonian SSR, against poliomyelitis, 9.6, and against diphtheria 12.8, whereas these figures in the Uzbek SSR were 0.45, 0.57, and 0.65, respectively, which speaks to diverse interpretations on the part of medical workers of the contraindications to inoculations [2].

It is entirely evident that Soviet public health workers at the present time have been compelled to deal with an extremely wide, clearly excessive list of contraindications, as a result of which the number of children receiving inoculations in the later periods, or not receiving them, is too high (according to our calculations from 800,000 - 1,000,000 annually). At the same time, the experience of a number of countries, of the United States, Great Britain, France, and others, as well as the experience of the WHO, which was accumulated within the framework of the Expanded Programme on Immunization (EPI), created with the support of the USSR in 1974, indicates that a large number of "traditional" contraindications are not contraindications in fact. Included in these are mild febrile states, diarrhea, the overwhelming majority of chronic noninfectious diseases, a number of allergic conditions, mild respiratory infections, etc. [10]. Naturally, it is practically impossible (and indeed hardly advisable) to attempt to work out universal recommendations in this regard. On the other hand, the EPI recommends to the member countries of WHO that they adhere to certain principles relative to the approaches to the treatment of contraindications to inoculations. We shall presume that these are of interest for our public health sector:

—public health workers should use all available capacities for the immunization of children in whom there are no contraindications;

—a slight increase in body temperature, mild respiratory infections, diarrhea, and other mild illnesses should not serve as contraindications to vaccination;

—above all, children with inadequate nutrition require vaccination;

—if a child who has received one or two doses of DPT shows severe side reactions, it is necessary to drop the next dose of the vaccine, and replace it with DT, completing the course of immunization;

—the decision regarding the immunization of sick children who require hospitalization is made by the hospital physicians, based on the vaccination status of the child (when needed, they should assure the vaccination of discharged patients, etc.);

At the same time, it should be kept in mind that risk of serious complications resulting from vaccination is significantly less than the danger from complications from naturally acquired infections (see Table 1);

In developing the policy regarding this question, it is also necessary to pay attention to the fact that the vaccination of children in risk groups is accompanied by antibody-formation which does not differ from that in essentially healthy inoculated children.

Table 1. Comparative Data on the Frequency of Complications in Illness From Some Target Infections and in Vaccinations Against Them

Vaccine	Types of Complications	Complications	
		in the case of illness (per 100,00 cases)	in the case of vaccination (per 100,00 inoculated individuals)
BCG	Disseminated tuberculosis	-	0.1
	Osteitis (osteomyelitis)	-	0.1-30
	Purulent lymphadenitis	-	100-4300
DPT	Fixed cerebral disorders (pertussis)	600-2000	0.2-0.6
	Encephalitis (encephalopathy)	900-4000	0.1-3.0
	Convulsions	100-8000	0.3-90
	Shock	-	0.5-30
	Lethal outcome	100-4000	0.2
Live measles vaccine	Encephalitis (encephalopathy)	50-400	0.1
	Subacute sclerosing panencephalitis	0.2-2.0	0.05-0.1
	Pneumonia	3800-7300	-
	Convulsions	500-1000	0.02-190
Oral live poliomyelitis vaccine	Paralytic form of poliomyelitis	500	9.1

The steps which have been taken repeatedly by the USSR Ministry of Health to review the contraindications to inoculations have not led to any substantial changes, due to the fact that the cautiousness which is traditional in this respect for our pediatricians always has the upper hand. At the same time, this cautiousness, in the practically total absence at the present time of a broad-based explanatory effort among the population, and particularly among parents, may lead to highly unfortunate consequences. The experience of Great Britain and Japan has shown that a decrease in the health education effort among the population in the presence of heightened cautiousness of physicians in the interpretation of the contraindications to inoculations with the DPT vaccine has been resulting in outbreaks of morbidity from pertussis [5]. Taking this fact into account, and attending to the increasing trend in our country of parents refusing the immunization of their children under the impact of the publication of dubious data regarding complications resulting from the use of certain vaccines, it is necessary to restructure the health education effort in this regard, by making it one of the principal objectives of the work of the district pediatrician. Our system of vaccinal prevention requires review of other organizational principles of carrying out vaccination operations as well, for the purpose of increasing their effectiveness. It seems advisable in this connection to clearly divide the responsibility for this effort between the pediatric and sanitary-epidemiological services. It is necessary to entrust the district pediatrician, who is obligated to carry the full responsibility for the timely vaccination for each child in his district, with the planning and carrying out of inoculations. This being the case, the vaccination operations should be regarded as one of the principal criteria for evaluating the work of the pediatrician. In this case, the district physician will monitor daily the list of children who are subject to vaccination in his district, and, proceeding from a plan of inoculations, carry out the work to improve the health of children with temporary contraindications and to

subsequently vaccinate on a timely basis. Since the number of children with persistent contraindications in the country as a whole, according to our data, does not exceed 1 percent, and throughout the republics ranges from 0.12 - 2.3 percent in the group of children up to one year of age, from 0.11 - 1.28 percent in the group of children up to two years, and from 0.076 - 0.77 percent in the group of children up to the age of three years; there is reason to assume that the aforementioned coverage of children subject to vaccination with inoculations may perceptibly increase. At the same time, the sanitary-epidemiological service should take on itself the monitoring of the vaccination operations as a whole.

In the majority of the world's countries, including the USSR, a standard set of monovalent and combined vaccines are used within the framework of national immunization programs: the BCG and the DPT, measles, and poliomyelitis vaccines; and mumps vaccine and German measles vaccine have been more and more widely used in recent times. These have been used both in the form of monovalent vaccines, as well as in the form of a combined measles-mumps-German measles vaccine. Other vaccines have been employed as well in a number of countries within the framework of routine vaccination (against yellow fever, hepatitis B, etc.).

In order for all of the vaccinal preparations enumerated, and others, to retain their immunogenic properties strict observation is required of the necessary temperature conditions during their transport and storage along the entire path of their "movement" from the enterprise which manufactured the preparations to the individual to be vaccinated. Violation of these conditions leads to partial, and sometimes complete, loss by the vaccines of their activity, as a result of which a certain proportion of those individuals vaccinated with such vaccines remain unprotected against the corresponding infections; hence a high level of morbidity from these infections.

This problem can be solved by the creation of an effective cold chain system, such has already been widely introduced by the WHO in the practice of national immunization programs. This system subsumes three basic components:

—specially trained personnel, upon whom the servicing and the correct maintenance of cooling equipment, and the storage and distribution of vaccines depend;

—the refrigeration equipment for the storage and transport of vaccines;

—the equipment and the control system for the observation of the temperature conditions at all stages of the cold chain.

Along these lines, it is above all necessary to achieve a sharp change in the attitude toward the cold chain on the part of medical personnel at all levels, from managers to staff who deal directly with the carrying out of vaccinations. It is necessary that each person know that without a clearly functioning cold chain vaccinal prevention cannot be effective. This may be achieved only through the training and retraining of the relevant medical personnel. According to our calculations, approximately 150,000 specialists in our country should undergo such training.

In this country we usually use the cold chain equipment which was produced for general use in everyday life. At the same time, the experience of the WHO and many of its member nations tells a different story: special thermal containers for single or multiple use, in which vaccines can be stored at 4 - 8°C from 2 - 7 days, special cold-storage pouches, etc. are required for the successful functioning of the cold chain. The temperature in these vessels is maintained by the placement in them of cooling elements previously frozen in a freezer. It is especially necessary to emphasize the importance of single-use thermal containers for the transport of vaccines from the manufacturing enterprises to the republic, kray, oblast, and municipal sanitary-epidemiological stations, where a large number of preparations, the spoilage of which could lead to excessive losses, are delivered simultaneously. As Soviet experience shows, the utilization of the standard packing crates for these purposes not only does not answer to the elementary requirements, but is also not cost effective. Thus, the setting up in the USSR of the production of thermal containers and of other equipment for the transport of vaccines is an urgent objective. The ordinary cold-storage pouches which we produce at the present time unfortunately do not meet the requirements of the cold chain.

A preliminary analysis of the state of the cold chain in a number of territories of our country, carried out by the Central Scientific Research Institute of Epidemiology, USSR Ministry of Health, showed that for some regions of the USSR in which electrical power is either not accessible or is delivered with great irregularity, refrigerators which operate on kerosene or gas are necessary. Such refrigerators are approved by the WHO and are widely utilized in a number of countries and regions of the world.

In order to assess the effectiveness of the functioning of the cold chain, the various indices recommended by the WHO are used at the present time. The use of these indicators make it possible to identify, rapidly and simply, deficiencies in the system of the cold chain, and to determine the possibility of using one preparation or another. There are indicators which determine the levels of the elevation of temperature at various stages of the "movement" of the vaccines along the cold chain, as well as their possible freezing, which is important for adsorbed preparations, since the latter also lose their immunogenic properties when frozen. In addition, the use of indicators, among which the control indicator card has received the greatest acceptance abroad, makes it possible in the majority of cases to get by without biological monitoring of the quality of vaccines, which is not only costly in labor, but is also very expensive [6].

Numerous publications regarding the increased level of morbidity among vaccinated individuals in various regions of the USSR tell of the kinds of negative consequences the violation of the temperature conditions for the storage and transport of vaccinal preparations can lead to. We would like in this connection to emphasize the particular importance of the publication of the conjoint order of the USSR Ministry of Health and the USSR Ministry of the Medical and Microbiological Industry of 18 November 1988, "On the Organization on the Territory of the Country of a Cold Chain System in the Transport and Storage of Medical Immunobiological Preparations", in relation to the development of which domestically produced, single- and multiple-use thermal containers are being developed, as well as the fact that education-methodological materials on the cold chain have been worked out by personnel of the USSR Ministry of Health Central Scientific Research Institute of Epidemiology for the training of medical personnel of various levels, and that training courses on this topic are already being conducted.

Substantial untapped resources reside in the perfection of the schedule of inoculations. This subsumes not only the obvious change in the schedule which comes about as the result of the introduction of fundamentally new or significantly improved vaccinal preparations into practice, but the urgent need for the development of scientifically-based alternate schedules for different regions of the country. The inoculation schedules currently in use in various countries are characterized by great diversity; these all possess serious scientific substantiation. In the process the specific features of the epidemic situation in the region, the immunoreactivity of the children who are subject to vaccination, as well as the climatic and socioeconomic characteristics are all taken into account.

It has been possible to recommend to the developing countries, based on the experience of the WHO, accumulated over the course of the more than 10 years' existence of the EPI, a very simple schedule, in which DPT and the live poliomyelitis vaccine are prescribed simultaneously three times, starting by the age of six weeks, with an interval of four weeks; the BCG vaccine is prescribed at birth, when a dose of live poliomyelitis vaccine can be additionally prescribed on the basis of epidemic indications. Live measles vaccine is introduced at the ninth month of age, and in certain countries (Zambia, China, Albania) even at the eighth month of age. There have recently been encouraging results indicating the possibility of the utilization of measles vaccine obtained from the Edmonston-Zagreb strain at earlier periods. At the same time, the measles vaccine is not given before the age of 12 months in countries with a predominantly continental climate. The question of revaccination has not been resolved unequivocally. The policy of the WHO on this problem reduces to the fact that if the coverage of child population is less than 80 percent, revaccination is inadvisable. On the other hand, it is believed that a one-time use of the standard measles vaccine and three to four doses of live poliomyelitis vaccine is sufficient for the development of lifetime immunity in the inoculated individual [9]. At the same time, in a large group of countries in Europe and North America, revaccination is obligatory [11]. To a certain degree, due to the specifics of the schedule of inoculations developed for particular regions, it has been possible by now to achieve very impressive successes in the campaign against controllable diseases. It is enough to note that while the level of the coverage of child population with inoculations had not exceeded 10 percent by the middle of the 1970s, by 1989, i. e., 15 years after the beginning of the implementation of the EPI, the coverage with DPT and poliomyelitis vaccine had reached 66 percent, i. e., practically the same level as in economically developed countries. The coverage with BCG in the developing countries (72 percent) was even higher than in the developed countries (59 percent), and only the coverage with inoculations against measles was lower (59 percent) than in the developed countries (76 percent). In addition, according to the WHO's assessment, thanks to the carrying out of vaccinal prevention it was possible to prevent 335,000 cases of poliomyelitis, 63,141,000 cases of measles and 1,353,000 lethal cases of measles, as well as 51,209,000 cases of pertussis and 446,00 fatal outcomes from this disease, in the developing countries in 1989 alone; it was also possible to prevent 356,000 fatal outcomes from tetanus of the newborn [8].

In the USSR, from the time that planned vaccinal prevention was introduced into Soviet public health practice, the inoculation operation has been conducted according to a uniform schedule for the entire country, although there are regions on the vast territory of the USSR which differ significantly from one another. Without dwelling upon the characteristics of the inoculation schedule employed at the present time in the USSR, in keeping with international experience we would like to draw attention to the urgent the necessity of developing alternate regional inoculation schedules; this, in all probability, is needed first and foremost by the republics of Central Asia, the Transcaucasus, etc.

The development of such schedules requires the carrying of additional research to study the immune response of children inoculated with various vaccines and at various periods, as well as the effectiveness of new mixed vaccines: vaccines against measles, mumps, german measles, etc. The study of the problems of revaccination deserves special attention, focusing on the experience of the WHO and a large number of countries.

The above does not exhaust the list of problems associated with the inoculation operations. The necessity of producing strictly standard vaccines must be mentioned among these, since the experience of the Central Scientific Research Institute of Epidemiology, USSR Ministry of Health, as well as data obtained at the WHO, attest to the fact that some of our vaccines do not meet contemporary international evaluation criteria. It suffices to mention that in 1989 alone that more than 20 percent of BCG vaccines were rejected in the control process, and

in connection with the fact that the measles vaccine did not meet the imposed requirements, its production was shut down in 1988, and its delivery was decreased by 75 percent. The situation with respect to live poliomyelitis vaccine is no better, about 15 percent of which was rejected in 1989 due to its low specificity. This is explained by the low technical instrumentation of the production facilities, the poor quality of the filling and sealing of the ampules, as well as the low quality of the monitoring of the products, etc. The latter raises the question of the necessity of the fundamental change in our country in the methods and mechanisms, as far as biological and epidemiological control of the quality of vaccines. The improvement of this situation will in many ways inhibit the monopolism in the production of immunobiological preparations in our country; without the introduction of alternative production of these preparations, it will probably be quite difficult to solve this problem.

Increasing the effectiveness of the campaign against controllable infections also requires the universal introduction of epidemiological oversight of these infections and their vaccinal prevention. In the process it is necessary to strive toward the broad introduction of immunological methods of control of the inoculation status and the state of protection in relation to these infections as an inseparable part of the system of epidemiological control of infections which are controllable by specific prophylaxis.

It is apparently not completely realistic to raise the question of the further reduction of morbidity from the above-mentioned infections, not to speak of elimination of some of these, without resolution of the problems indicated above.

FOOTNOTES

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Concerning Capacity of Some Microorganisms to Synthesize Porphyrins on Water-Insoluble Substrates

907C0847A Kiev MIKROBIOLOGICHESKIY ZHURNAL in Russian Vol 52 No 3, May-Jun pp 28-30

[Article by T. V. Vygovskaya, N. M. Datsyuk and S. A. Yeliseyev; Lvov State University; Departmment of Physical Chemistry and Technology of Combustible Minerals; UkSSR Academy of Sciences Institute of Physical Chemistry, Lvov]

UDC 579.222'117.3

[Abstract] A study of the capacity of bacteria Propionibacterium shermanii, Pseudomonas fluorescens and Rhodococcus sp. to synthesize porphyrins during cultivation on water-insoluble carbon substrates used a 2 percent mixture of n-paraffins (C_{12} - C_{14}) and Lvov Fat Combine wastes containing 85 percent palmitic acid in a concentration of 1 percent by volume as a carbon source. Cultivation proceeded under aerobic conditions at 30°C for 7 days. The bacteria synthesized both extracellular and intracellular porphyrins without addition of an exogeneous precursor during cultivation on media containing carbons. The high cost of the biogenetic precursor of porphyrins synthesis, ΔALK, and the relatively low cost of the hydrocarbon raw material suggested that development of a biotechnological process of producing microbial tetrapyrrols will be profitable. References 5: 2 Russian, 3 Western.

Effect of Magnetic Field on Bacterial Leaching of Manganese

907C0847B Kiev MIKROBIOLOGICHESKIY ZHURNAL in Russian Vol 52 No 3, May-Jun 90 pp 84-88

[Article by G. I. Tyrugina and V. S. Savchuk; Dnepropetrovsk State University]

UDC 579.69:669

[Abstract] A study of the effect of a 50 - 150 Oe permanent magnetic field on bacterial leaching of manganese from ore from the Nikopolskiy deposit and a study of the dynamics of formation of acid and peroxide metabolites participating in degradation of manganese ores and removal of soluble forms of manganese into the environnment showed that treatment of ore pulp by a magnetic field of 100 Oe for 3 minutes increased production of the manganese-leaching strain 182-A of acid and peroxide metabolites, which participate in degradation of manganese ores, and the bacterial removal of manganese from ore 1.4 - 2.8 times. Figure 1; references 15: 14 Russian, 1 Western.

Antibiotic-Resistant Klebsiella sp. From Coastal Waters of Caspian and Baltic Seas

917C0044B Moscow ANTIBIOTIKI I KHIMIOTERAPIYA in Russian Vol 35 No 6, Jun 90 (manuscript received 20 Apr 89) pp 24-26

[Article by N. N. Moyseyenko, Moscow Scientific Research Institute of Hygiene imeni F. F. Erisman]

UDC 579.842.16:579.252.55:615.33]:551.468.2/.3[261.24+262.81]

[Abstract] The distribution of antibiotic resistant strains of Klebsiella was studied in recreational water consumption areas of the Caspian and Baltic seas, as well as in areas affected by agricultural waste water. Sixteen samples from eight Baltic sea sites and twelve samples from six Caspian sea sites were tested. All but one of the samples were positive for Klebsiella. In the Baltic samples resistance to carbenicillin was most common, followed by ampicillin, chloramphenicol, streptomycin, tetracycline, kanamycin, gentamycin, cephazoline, nalidixic acid and rifamycin. The percentage of resistance ranged from 40 percent to 0.4 percent. The results were slightly different for Caspian samples. Resistance to ampicillin was most common, at 74 percent, followed by carbenicillin, cephazoline, streptomycin, tetracycline, chloramphenicol, nalidixic acid, and kanamycin. No strains resistant to gentamycin or rifamycin were seen in Caspian samples. A statistically significant difference was seen between the two sources; 86 percent of the Caspian strains and 70 percent of the Baltic strains were resistant to at least one antibiotic. No differences between recreational areas and entry points for agricultural waste water were observed. Among the 134 strains isolated from the Caspian sea, 29 different combinations of antibiotic resistance were seen. For the 197 Baltic strains, 41 different combinations were noted. Fifty multiple resistant Baltic strains were tested for the conjugative R-plasmid, which was found in 20 of them. Thirty-one Caspian strains were tested and eighteen had the plasmid. Of the 38 strains resistant to three antibiotics tested, the plasmid was seen in 20. Four strains with high rates of multiple resistance transfer were found. The results indicate that antibiotic-resistant Klebsiella are widespread in the Baltic and Caspian seas. Figures 1; references 20: 1 Russian, 19 Western.

Antibiotic Sensitivity in Shigella Isolated During 1987-1988 in Karakalpak ASSR

917C0044C Moscow ANTIBIOTIKI I KHIMIOTERAPIYA in Russian Vol 35 No 6, Jun 90 (manuscript received 15 Aug 89) pp 27-29

[Article by V. A. Shenderovich, O. S. Saparov, L. F. Bagdanova, V. Ye. Solovyeva, I. V. Vlasova, L. G. Stolyarova, N. I. Givental, Yu. F. Shcherbak, and Ye. A. Vedmina, Central Order of Lenin Institute for Advanced Training of Physicians, Moscow]

UDC 579.842.15:579.252.55:615.33][575.172]"1987-1988"

[Abstract] The antibiotic sensitivity of 61 Shigella strains isolated at one hospital in the city of Nukus in 1987-1988 was studied and compared to results obtained in previous years. Fourteen of the isolates were Shigella dysenteriae 1, which had not been observed previously at that site. The strains were most sensitive to cephotaxin, cephaloridine, polymixin, and gentamycin. Most isolates were resistant to ampicillin and carbenicillin; all showed some resistance to erythromycin and rifamycin. Sensitivity to tetracycline, levomycin, and streptomycin was unchanged in 1987-1988, compared with 1984-1985, while sensitivity to the aminoglycosides neomycin, kanamycin, and gentamycin, and to ampicillin and carbenicillin was somewhat increased. Sensitivity to cephaloridine tended to decrease from 1984 to 1988. S. dysenteriae 1 was resistant to tetracycline, levomycin, and streptomycin, at levels similar to the most prevalent Shigella, S. flexneri 1-5. S. dysenteriae 1 remained more sensitive to ampicillin and carbenicillin than S. flexneri 1-5. References 8: 4 Russian, 4 Western.

In Vitro Activity of Antibacterial Drugs Against Causative Agent of Pseudotuberculosis

917C0044D Moscow ANTIBIOTIKI I KHIMIOTERAPIYA in Russian Vol 35 No 6, Jun 90 (manuscript received 17 Jul 89) pp 29-31

[Article by P. G. Vasilev, V. B. Kalininskiy, N. T. Vasilev, and A. V. Yurchenko, Scientific Research Institute of Microbiology, USSR Ministry of Defense, Kirov]

UDC 615.33.036.8:579.842.23

[Abstract] The sensitivity of 15 Yersinia pseudotuberculosis strains was tested in vitro using 32 antibacterial agents, in order to screen for promising in vivo agents. Twelve of the strains were sensitive to penicillin, cephalosporins, aztreonam, aminoglycosides, tetracycline, chloramphenicol, rifamycin, phosphomycin, quinolocarboxylic acids, and sulfamethoxazole with trimethoprim. Cephtizoxime, cephotaxime, gentamycin, and amikacin were the most active, as well as aztreonam, doxycycline and ciprofloxacin. Chloramphenicol, rifamycin, and tetracycline had markedly less activity. Three strains were isolated which were resistant to penicillin, cephalosporins, aminoglycosides and other antibiotics. There were some differences in sensitivity to cephalosporins and aminoglycosides among the resistant strains. The fluorine-derivitized quinolocarboxylic acids ciprofloxacin, norfolxacin, and enoxacin, as well as tetracyclines, netylmycin, amikacin, cephotaxine, and cephazoline showed the broadest spectrum of activity against pseudotuberculosis. References 5: Russian.

Synthetic Human Interleukin-2 Gene Reconstruction

917C0024A Moscow BIOORGANICHESKAYA KHIMIYA in Russian Vol 16 No 6, Jun 90 (manuscript received 26 Jun 89) pp 759-764

[S. V. Seregin, V. A. Ryabinin, A. N. Sinyakov, N. K. Danilyuk, and S. G. Pozdnyakov, All-Union Molecular Biology Scientific Research Institute, "Vektor" Scientific Industrial Association, Koltsovo, Novosibirsk Oblast]

UDC 577.113.6

[Abstract] Chemico-enzymatic synthesis and cloning of the DNA fragment that codes for the signal sequence of the human interleukin-2 (IL-2) gene were investigated as a means of reconstructing a synthetic IL-2 gene in genetic structures capable of secreting IL-2 and its analogs in eukaryotic expression systems that are also suitable for creating chimeric proteins. The hybrid pSIL-2 plasmid that was obtained carried the human IL-2 gene with the signal sequence and exhibited effective expression in eukaryotic systems. In addition, reconstruction of the pIL-2 plasmid that permits removal of terminal IL-2 gene codons was performed to construct chimeric genes that have the IL-2 sequence at the 5' end. Merits of the synthetic IL-2 gene include the large number of restriction endonuclease sites surrounding the gene and the ease with which it can be transferred into various vectors and joined with practically any regulator element. It is hoped that these advances will lead to the creation of proteins based on IL-2 with a new range of properties. Figures 3; references 18: 5 Russian, 13 Western.

Sanitary Protective and Limitation Zones for Antennas of Decameter Range

917C0075B Moscow GIGIYENA I SANITARIYA in Russian No 7, Jul 90 pp 53-56

[Article by Yu. D. Dumanskiy, Yu. M. Spodobayev, S. V. Bitkin et al.; Kiev Scientific Research Institute of General and Public Hygiene imeni A. N. Marzeyev]

UDC 613.167/.168-07

[Abstract] An examination of transmitting antennas of the decameter range showed that the structure of the electromagnetic field near the antenna is exceptionally complex and depends upon so many factors that it is impossible to consider all of them in order to make sufficiently accurate predictions. Inadequacies in the system used by the Ministry of Communications USSR (based on Bendenskiy's classical interference formula) and the system using the Shuleykina-Van-der-Pol formula were mentioned and discussed briefly. The studies showed that the most accurate method of calculated prediction is the method developed at Kuybyshev Electrical Engineering Institute which is a system of automatic prediction of the electromagnetic situation. This method was described and discussed. The boundary of sanitary-protective zones and zones of limitations were found to depend upon the antenna wavelength, the radiated power and the type of soil involved. Figures 4; references 3: Russian.

New Antiviral Compound Tested

917C0011A Vilnius EKHO LITVY in Russian 13 Jul 1990 pp 2-3

[Article picked up from ELTA news agency, Baltiya: "Will a Check Be Found for Viruses?"]

[Text] A compound possessing stronger antiviral activity than any existing medical preparation has been produced by the joint efforts of the workers of the Institute of Organic Synthesis of the Latvian Academy of Sciences and the Sverdlovsk Polytechnical Institute.

The substance, for now called tetracyclane, acts, as it was ascertained, on various types and strains of variable flu pathogens. It blocks their reproduction by binding with protein envelopes. Numerous experiments on cell cultures and animals have given encouraging results. In the opinion of scientists, one can expect that further investigations will lead to the development of a universal preparation for the prophylaxis and the treatment of an infectious disease which has almost become the most widespread.

However, the experiments with this new compound are not limited to that. The specialists have detected under laboratory conditions that it also has the capacity to withstand the viruses of tickborne encephalitis and even AIDS.

Anticholinesterase Activity of Berberine and Its Synthetic Analogs

917C0060C Dushanbe ZDRAVOOKHRANENIYE TADZHIKISTANA in Russian No 3, May-Jun 90 pp 81-83

[Article by Ye. Yu. Potapova, K. Kh. Khaydarov, A. V. Gulin and A. A. Linchevskaya; Central Scientific Research Laboratory, Pharamacological Laboratory of the Institute of Chemistry, Tadzhik SSSR Academy of Sciences]

[Abstract] A study of the anticholinesterase activity of berberine, beroline and berberrubine in anesthesized cats by the H. Dale method showed the greatest anticholinesterase activity in beroline. A subsequent comparative study of anticholinesterase activity of beroline and proserine on 3 - 5 g Chinchilla rabbits showed the pronounced and prolonged anticholinesterase effect of beroline which exceeded the short term effect of proserine which reached a peak in the first two hours after injection. The breadth of therapeutic effect: ratio of LD_{50} to ED_{50} (anticholinesterase activity) provided an indicator of the practical suitability of the preparations. The qualitatively new pharmacological activity of berberine and its synthetic analogs suggested that these drugs will find practical use as drugs which act on the peripheral mediator processes and augment the arsenal of anticholinesterase drugs. References 5: 4 Russian, 1 Western.

Spatial Selectivity of Vestibular Receptive Fields of Cerebellum Purkinje Cells Toward Orientation of Angular Accelerations

907C0849A Moscow BIOFIZIKA in Russian Vol 35 No 3, May-Jun 90 pp 489-493

[Article by V. M. Gusev and L. A. Semenov; Institute of Physiology imeni I. P. Pavlov; USSR Academy of Sciences; Leningrad]

[Abstract] A study of characteristics of orientational sensitivity of receptive fields of cerebellum Purkinje cells to angular acceleration involved microcaloric stimulation of the semicircular canals of the frog vestibular apparatus. Characteristics of transformations of signals realized in the vestibular receptive field of Purkinje cells had clearly pronounced spatial selectivity in relation to orientation of angular acceleration acting on the vestibular apparatus and in dependence upon its values. Maximal sensitivity of the vestibular receptive field to oscillating acceleration having fixed orientation in space was typical of small levels of acting angular acceleration. Transformations of the vestibular receptive field became more susceptible to the effect of angular acceleration cyclically changing its orientation in space in proportion to the level of angular acceleration. Figures 2; references 6: 5 Russian, 1 Western.

Dermorphine and Processes of Higher Nervous Activity in Insectivores

917C0048C Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 313 No 4, Aug 90 pp 1010-1015

[Article by A. I. Karamyan, deceased, T. N. Sollertinskaya and E. N. Nuritdinov; Institute of Evolutionary Physiology and Biochemistry imeni I. M. Sechenov; USSR Academy of Sciences; Leningrad]

[Abstract] A study of the effect of dermorphine on the conditioned reflex activity of insectivores, hedgehogs, the lowest of the hibernating animals, involved examination of food-procurement behavior of nine long-eared Central Asian hedgehogs. The study included consideration of positive conditioned reflexes, different forms of internal inhibition and changes of these forms of nervous activity after subcutaneous injection of dermorphine (0.1mg/kg directly before the experiment). Injection of dermorphine produced the typical analgesic effect and a significant effect on the functional state of the hedgehogs. It produced significant changes in innate and inherited forms of nervous activity with greatest effect on processes of internal inhibition. The reasons for this effect of dermorphine on the higher nervous activity were discussed briefly and will be considered further in future reports of the effect of dermorphine on hibernating and non-hibernating rodents. References 15: 6 Russian, 9 Western.

Biorhythms and Working Capacity of Sailors Under Conditions of Hypokinesia

917C0084 Moscow VOYENNO-MEDITSINSKIY ZHURNAL in Russian No 7, Jul 90 pp 64-65

[Article by O. Yu. Netudykhatka, A. I. Akulinin, candidates of medical sciences, and A. P. Stoyanov and V. G. Kravets]

UDC 613.6:656.61

[Abstract] A study is made of the dynamics of biorhythms of bodily functions and performance of sailors in a physical training program on transmeridional cruises. Sixty-two sailors 20 - 45 years of age were studied; 32 exercised, while 30 did not, on cruises crossing one to eight time zones. It was found that the sailors involved in active physical training experienced less difficulty in crossing the time zones. Motor activity facilitates more rapid adjustment of physiological functions, greater resistance to unfavorable environmental effects and better preservation of efficiency.

Atropine-Like Effect (Not Removed by Naloxone) of Opioid Dermorphine on Inotropic Effects of Acetylcholine

917C0132 Moscow BIOLOGICHESKIYE NAUKI in Russian No 10, 90 pp 80-85

[Article by N. A. Sokolova, V. G. Krasilnikova and I. P. Ashmarin]

UDC 612.178:591.112

[Abstract] Experiments on isolated frog heart, perfused by the Straube method, showed that dermorphine caused negative inotropic effect which was blocked by naloxone. Against the background of negative inotropic effect of dermorphine, acetylcholine suppressed ventricular contractile activity to the same degree as that which existed before injection of dermorphine. Acetylcholine, injected against a background of combined effect of dermorphine and naloxone, eliminated the natural inotropic effect of the opioid and the negative inotropic effect became much weaker than the initial effect. There were assumed to be opiate receptors in the frog ventricular myocardium and the activation of these caused development of a negative inotropic effect. Dermorphine produced an atropine-like effect on the inotropic effects of acetylcholine. The effect did not depend on activation of the opiate receptors. Figures 3; references 11: 3 Russian, 8 Western.

Effect of GABA Agonists and Bicuculline on Carp Electroretinogram During Adaptation to Dark and Background Illumination

917C0137A Moscow VESTNIK MOSKOVSKOGO UNIVERSITETA: BIOLOGIYA in Russian No 3, Jul-Sep 90 (Manuscript Received 22 Jan 90) pp 49-55

[Article by N. S. Garina and V. G. Yerchenkov]

UDC 612.843.215

[Abstract] Experiments on 38 intact carp tested the effect of application to the retina of gamma-amino-butyric acid [GABA] agonists (muscimol and baklophene) and antagonist (bicuculline) on the electroretinogram evoked by white light and monochromatic light. All these substances decreased the amplitude of the b-wave. Muscimol suppressed the b-waves after adaptation to the dark and to background illumination. Bicuculline and baklophene were effective only for an electroretinogram caused by exposure to white and green light (λ = 50 nm). After adaptation to background illumination, the effects of bicuculline and baklophene did not depend on the wave length of the light stimulus but increased the amplitudes of the a-, b- and d-waves. Muscimol, after adaptation to illumination, suppressed the b-wave but its effect on the electroretinogram caused by exposures to red light (λ = 658 mn) was unreliable. Since the electroretinogram, after adaptation to background illumination, is determined to a lesser degree by activity of the rod system than after adaptation to the dark, it was assumed that the effects evoked were caused predominantly by the effect of the substances on the rod and cone system activity that predominate in darkness and against a background of light, respectively. References 17: 2 Russian, 15 Western.

Assessment of Effectiveness of Biotechnological Breakdown of Anionic Surfactants With Aid of Biological Tests

917C0137B Moscow VESTNIK MOSKOVSKOGO UNIVERSITETA: BIOLOGIYA in Russian No 3, Jul-Sep 90 pp 74-78

[Article by S. A. Ostroumov and L. S. Samoylenko]

UDC 574.64:556.531.4

[Abstract] A bioreactor with immobilized Pseudomonas mendocina 2 S cells was used to purify water containing sulfonol (0.1 g/l). The effectiveness of water purification was monitored by using a chemical method of biological testing. Biological testing was applied to Fagopyrum esculentum, Lepidium sativa and Sinapis alba. Polluted water, not purified, inhibited growth of seedlings of all three species. Purification by the method described in the article improved the water quality greatly and the response of the seedlings of all three species improved significantly. The method is relatively inexpensive and may be used to purify water contaminated by other xenobiotics. Figures 1; References 6: 4 Russian, 2 Western.

Hyperbaric Oxygenation in Experimental Acute Cerebral Compression-Displacement Syndrome: Histological Assessment

917C0171A Moscow ZHURNAL NEVROPATOLOGII I PSIKHIATRII IMENI S.S. KORSAKOVA in Russian Vol 90 No 10, Oct 90 (manuscript received 01 Aug 89) pp 27-32

[Article by B. M. Livshits, Yu. V. Isakov and I. G. Lyudkovskaya, Department of Hyperbaric Oxygenation,

Scientific Research Institute of Emergency Medicine imeni N. V. Sklifosovskiy, Moscow; Laboratory of Pathologic Anatomy, Scientific Research Institute of Neurology, USSR Academy of Medical Sciences, Moscow]

UDC 616.831-001.35-036.11-085.835.3-092.9

[Abstract] Experiments were carried out on 2.5 - 3.8 kg chinchilla rabbits to assess the efficacy of hyperbaric oxygenation (HO) in alleviating cerebral damage due to compression and displacement. Brain compression was induced by the epidural balloon technique and maintained for either < 12 h or > 12 h, followed by HO management. The results of clinical observations and histological studies demonstrated that 2 - 4 HO sessions (1.6 atm 30 min) in the first 24 h, with a maximum of 10 sessions over a 4 day period, reduced mortality and attenuated hyperextension. The reduction in mortality was accompanied by reduction of edematous changes in the cortex, white substance and the brain stem and alleviation of venous stasis. In the final analysis, the beneficial effects of HO in brain damage were attributed to reduction in intracranial pressure and mitigation of cerebral hypoxia. Figures 6; references 17: 10 Russian, 7 Western.

Isolation, Purification and Structure of Vasoactive Molecule From Rabbit Skeletal Muscles

917C0210A Moscow BIOKHIMIYA in Russian Vol 55 No 12, Dec 90 (manuscript received 15 Jan 90; in final form 22 Mar 90) pp 2138-2147

[Article by G. G. Petrovskiy and E. P. Titovets, Belorussian Scientific Research Institute of Neurology, Neurosurgery and Physical Therapy, Minsk]

UDC 577.152.3

[Abstract] The full armamentarium of biochemical techniques were utilized for the isolation, purification and definition of the nature of a vasoactive component of rabbit skeletal muscles. Testing on rats has shown that the active principle induced a short-term hypotensive response that is eventually replaced by long-term hypertension. Information derived from UV, IR, ESR and ^{13}C-NMR spectroscopic analyses pointed to the vasoactive entity as an inosine nucleotide with a free phosphate group and di- and trialanine peptides at C-2 and C-3 of the pentose ring. Loss of activity at room temperature was evidently due to hydrolysis of the ester bonds and formation of inactive inosine phosphate. These findings suggest that purine nucleotides may exert a local vasoactive role. Figures 5; references 22: 13 Russian, 9 Western.

Affinity Characteristics of Monoclonal Antibodies in Solid Phase ELISA

917C0210B Moscow BIOKHIMIYA in Russian Vol 55 No 12, Dec 90 (manuscript received 25 Jan 90) pp 2163-2170

[Article by N. V. Yermakov, A. G. Ishkov, Ye. V. Miroshnichenko, O. P. Plyushch, E. N. Remizova, P. G. Sveshnikov, Ye. Yu. Chenchikova and N. G. Cherchenko, Scientific Center of Molecular Diagnostics, USSR Ministry of Health, Moscow]

UDC 575.11

[Abstract] Solid phase ELISA was used to assess affinity characteristics of BALB/C monoclonal antibodies (MA; IgG1) against porcine insulin (Ag) in order to assess the analytic possibilities of such combinations. Applying conventional Scatchard plots to the peroxidase-based ELISA yielded the following equation: $(Ag)_0 = (A_{405}/c_0)/tg\alpha$, where A_{405} is the OD and $tg\alpha$ is the tangent of the linear portion of the plot, i.e., the binding constant. The sensitivity of the technique was dependent on the binding constant, which ranged from 5 x 10E6 to 1.1 x 10E10 M^{-1}. The latter parameter was dependent on the temperature, pH and hydrophobization of the MA. The MAs were stable for 10 min at 60°C and tolerated a pH range of 4.12 - 10.84; at 37°C binding activity was retained for 60 min. The system was deemed suitable for determination of antibodies and antigens in biological samples. In addition, intact MAs or their F(ab) fragments may be used as delivery vehicles for bound ligands to biological target sites. Figures 3; tables 1; references 15: 3 Russian, 12 Western.

Comparative Enzymology of Meta-Cleavage of Aromatic Rings by Pseudomonads With Plasmid and Chromosomal Control of Biphenyl and m-Toluate Catabolism

917C0210C Moscow BIOKHIMIYA in Russian Vol 55 No 12, Dec 90 (manuscript received 5 Feb 90) pp 2171-2181

[Article by S. A. Selifonov and I. I. Starovoytov, Institute of Biochemistry and Physiology of Microorganisms, USSR Academy of Sciences, Pushchino, Moscow Oblast]

UDC 577.152.3

[Abstract] The presence of D-plasmids in pseudomonads has generated interest in the use of Pseudomonas sp. for pollution control, and has stimulated studies on the mechanisms of biphenyl degradation. Assays on Ps. putida strains bearing different plasmids has shown that regardless of whether biphenyl catabolism is under chromosomal or plasmid control two different enzymes are involved in meta-cleavage: 2,3-dihydroxybiphenyl-1,2-dioxygenase (I) and catechol-2,3-dioxygenase (II). Enzyme I has been shown to be most efficient in cleavage

of 2,3-dihydroxybiphenyl regardless of its origin, although it also exhibits some activity against 3-methylcatechol and catechol, but fails to cleave 4-methylcatechol. Enzyme II, however, has shown considerable substrate variation depending on the strain from which it was isolated. When encoded by plasmids pBS241 and pBS311 it displays moderate activity against catechol and 3-methyl- and 4-methylcatechols, but does not cleave 2,3-dihydroxybiphenyl. However, when under chromosomal control in Ps. putida BF and TOL-plasmid (pWWO) it cleaves all four substrates. Despite the fact that plasmids pBS241 and pBS311 have been originally isolated from different geographic areas and ecologic niches, the fact that they encode enzymes with identical properties in the case of enzymes I and II points to their close relatedness. Furthermore, chromosomally encoded enzyme II has a wider potential in pollution control than its plasmid encoded congener because of the former's broader activity spectrum. Figures 2; tables 5; references 24: 7 Russian, 17 Western.

Phospholipase A_2 and Lipid Peroxidation in Uncoupling Oxidative Phosphorylation in Rat Liver Mitochondria

917C0210D Moscow BIOKHIMIYA in Russian Vol 55 No 12, Dec 90 (manuscript received 19 Feb 90) pp 2195-2199

[Article by V. G. Gogvadze, N. N. Bruyetovetskiy and A. A. Zhukova, Institute of Biological Physics, USSR Academy of Sciences, Pushchino, Moscow Oblast]

UDC 577.152.3

[Abstract] Biochemical studies and determinations of membrane potentials in the case of hepatic mitochondrial preparations derived from 180 - 200 g male Wistar rats provided further understanding of the uncoupling mechanisms of oxidative phosphorylation. Uncoupling induced by cumene hydroperoxide was attributed to the products of lipid peroxidation (LP) in situations of calcium overload. Addition of phospholipase A_2 inhibitor—p-bromophenacyl bromide—prevented the decline in membrane potential and loss of calcium ions from the mitochondria, without affecting accumulation of LP products. The data lent themselves to the interpretation that the calcium-dependent phospholipase A_2 was activated in the course of LP and further accelerated uncoupling of oxidative phosphorylation. Figures 2; tables 1; references 15: 2 Russian, 13 Western.

Isolation, Purification and Properties of Cellobiohydrolases of Trichoderma Longibrachiatum

917C0210E Moscow BIOKHIMIYA in Russian Vol 55 No 12, Dec 90 (manuscript received 22 Mar 90) pp 2268-2273

[Article by O. V. Shpachenko, O. V. Yermolova and V. M. Chernoglazov, Chemical Faculty, Moscow State University imeni M. V. Lomonosov]

UDC 577.152.3

[Abstract] An analysis was conducted on the properties of cellobiohydrolase (EC 3.2.1.91) isolated from Trichoderma longibrachiatum, using a sequence of steps involving precipitation with ammonium sulfate and ion-exchange chromatography on DEAE-Spherone and Mono Q columns. The enzyme was found to have a MW of 65,000 D on polyacrylamide gel electrophoresis and 54,000 D on gel-filtration on TSK 4000PW, a pI of 3.7 and Henry's adsorption constant of 0.4 L/g on hydrocellulose, and to contain 1.6 percent carbohydrates. The highly purified cellobiohydrolase lacked endoglucanase activity, but cleaved CM-cellulose, beta-glucan, MUF-cellobioside, and amorphic and hydrocellulose with activities of 0.002, 0.006, 0.060, and 0.012 and 0.007 IU/mg, respectively. Figures 3; tables 1; references 19: 11 Russian, 8 Western.

Book: Psychophysiological Reactions of Energy Metabolism

917C0323A Riga PSIKHOFIZIOLOGICHESKIYE REAKTSII ENERGOOBMENA in Russian 89 pp 2, 3-8, 135 (signed to press 9 Oct 89)

[Annotation, foreword, introduction, and table of contents from book *Psikhofiziologicheskiye Reaktsii Energoobmena (Psychophysiological Reactions of Energy Metabolism)* by A. A. Aldersons, Latvian SSR Ministry of Health, Latvian Scientific Research Institute of Experimental and Clinical Medicine, Riga, Zinatne Publishing House, 1989, 1,100 copies, 135 pages]

[Text]

Annotation

This monograph sets forth the results of research on the role of higher nervous activity in man in the regulation of vegetative reactions of energy and heat metabolism. It puts forward the concept of the nature of psychophysiological reactions of energy and presents data on the interconnection of psychophysiological reactions with the process of activation and on the role of these reactions in the process of short-term adaptation.

This book is intended for physicians, physiologists, specialists in engineering psychology, sports medicine, labor physiology, and clothing physiology, and students at biological facilities and medical institutes.

12 illustrations; 266 bibliographic items.

FOREWORD

This monograph is the continuation of development of the subject, which we first generalized in the work "Mekhanizmy elektrodermalnykh reaktsiy" [Mechanisms of Electrodermal Reactions] published in 1985.

This book presents our own original point of view on the mechanisms of formation of psychophysiological vegetative reactions in their interconnection with energy

metabolism and thermoregulation. A scrupulous and systematic analysis of experimental material is not the author's task. Principal attention is concentrated on uncovering some inaccuracies in theoretical approaches to explaining the mechanisms of formation of psychophysiological vegetative reactions and alternative ways of overcoming a number of fundamental difficulties in their theoretical study and practical applications are proposed.

Since this problem has been little studied, the author's attempt to describe some flowsheets of mechanisms is inevitably connected with the pronouncement of a number of disputable and hypothetical propositions. The attempt to illuminate the problem concerning the mechanisms of formation of psychophysiological vegetative reactions of energy metabolism from the broadest possible aspect at times did not enable the author to dwell in detail on the presentation of the results of individual experiments.

In the style of presentation this book resembles rather a popular science publication and the author hopes that it will be accessible to quite a wide audience of readers interested in basic and applied problems of psychophysiology.

INTRODUCTION

The study of the dynamics of vegetative reactions occupies an important place in psychophysiology [24, 55, 59, 60, 63, 64, 80-82, 96-99, 103, 105, 116, 121, 124-126, 143, 165, 177, 186, 195, 200, 207, 221, 238, 249]. The registration of vegetative shifts makes it possible to objectively approach the analysis of psychic processes. This is important, because man's oral reports on the states experienced by him are not indisputable; a person can err sincerely, or distort facts consciously [80]. The dynamics of behavioral and vegetative reactions is virtually the only indicator of animal experiences. The application of physiological equipment in a physiological laboratory is aimed at singling out organic parameters, which lend themselves to a quantitative measurement, by means of which it is possible to make an objective reproduction of subjective psychological phenomena [80]. The need for the availability of reliable methods of objectivating the dynamics of a psychic state, in particular, for an objective control of the efficiency of a purposeful change (optimization) in a psychic state, is indisputable [3].

However, numerous attempts to use physiological methods in a psychological experiment and in practice encounter difficulties of a fundamental nature. As a result, despite the vast labor by researchers the problem cannot be considered solved. And although such an approach is widespread, in our opinion, the right to judge a psychic state by physiological reactions in general and by physiological vegetative reactions in particular is argued with insufficient seriousness. Such an approach is based rather on traditions and life observations than on scientifically substantiated opinions. In connection with this disputes concerning the scientific substantiation and objectivity of utilizing physiological, including vegetative, reactions for objectivating the dynamics of psychic processes do not end [75, 76, 78, 89, 92, 197].

Probably, the main difficulty is connected with the existence of a large number of psychological phenomena, on the one hand, and of the same large number of vegetative and other physiological reactions, which sometimes sharply differ in the biological sense, on the other, and the relationship established between them is of a statistical nature. Psychophysiologists have accumulated extensive experience in the application of such physiological indicators as the mosaic of the time-amplitude structure of activation of various muscular groups [32, 61, 62, 118], degree of synchronization of the electroencephalogram (EEG) of various leads [49, 69, 197], interhemispheric neurodynamics [28, 55, 57, 119, 197], and dynamics of correlations of hormones and mediators [95, 96].

The above-noted groups of psychophysiological indicators will not be examined in this work. On the one hand, in the frequency of application they are greatly inferior to another large group of psychophysiological reactions—vegetative reactions. On the other hand, we believe that at this moment it does not seem possible to unify them into one general system and to formulate general patterns in the reaction of each separately and all together in each specific life or experimental situation. We assume that, in principle, an endless increase in the number of such physiological reactions, which change when there is a change in a psychic state, is possible. The number of newly discovered neuromediators, neuropeptides, and new classes of substances modulating the action of mediators increases every year. In the last few years the multicomponent structure of synaptic receptors has been uncovered and it has also been established that in the descending tracts from the hypothalamus to the spinal cord the sympathetic system has a high degree of differentiation and so forth [3]. Such an essentially vast number of intermediary stages, the specific nature of each of which can affect numerical values and correlations (the functional structure) of the specific physiological indicators that are being studied, greatly hampers and sometimes makes it impossible to investigate regulating and controlling tactics of the organism and, at the same time, the characteristics of psychic processes and states through the registration and interpretation of various physiological indicators.

This work will discuss a group of physiological reactions most widely applied in psychophysiology—vegetative psychophysiological reactions. They also are not devoid of the above-noted shortcomings. There is no uniform opinion of the biological essence and adaptive significance of the ambiguously changing combination of various vegetative reactions during a change in a psychic state. Therefore, the choice of precisely these, not other, reactions in most experiments is justified inaccurately or is not justified at all and, partially, depends on the

researchers' technical capabilities and individual experience. In practice, researchers do not have a uniform opinion as to precisely which set of vegetative reactions should be applied in each specific experimental situation during the solution of each specific experimental problem [3].

The fact that various vegetative indicators do not change unidirectionally in different psychological situations [114] and patterns in the redistribution of activity among various vegetative, as well as between vegetative and behavioral, reactions are unknown [3] can be considered firmly established. It must be admitted that the basic principles arguing the right to judge the psyche in general and in each specific case in particular by vegetative reactions have not been formulated.

This work is an attempt to substantiate our idea of the mechanisms of formation of vegetative psychophysiological reactions participating in the energy and heat metabolism of the organism. Energy metabolism and thermoregulation, on the one hand, and psychophysiological vegetative reactions, on the other, can be considered a nontrivial variant of mutual relations among physiological functions. The functional interconnection among them has not been studied. At the same time, in our opinion, the problem of investigating this interconnection is exceptionally urgent for the following reasons:

1. The determining complexes of thermal and nonthermal parameters of the organism, according to the totality of which reactions of energy metabolism and heat exchange are turned on, turned off, and change the intensity and various patterns of their functional organization and structure, cannot be considered accurately and definitively established [2-4, 8, 10, 11, 34, 37, 67, 70, 163, 201, 224]. This indefiniteness is manifested in an especially pronounced manner under conditions close to thermoneutral ones [2, 5-7, 23, 112, 115]. There are descriptions of scrupulous research conducted for the purpose of accurately establishing such interrelations [134, 153-155, 192, 193, 203, 204, 228, 229, 232-234, 237, 261]. Often they are characterized by the input of a complex of formulas, which in most cases are applied only with a partial combination of the studied factors. An impression is created that increasingly more detailed and accurate research according to the applied stereotype will hardly lead to a full solution of the problem [10].

2. Some curious reactions and their complexes in thermoregulation, which to this day do not have a satisfactory explanation, are known. For example, research by V. A. Likhtenshteyn [70] notes that the equalizing and compensatory capacity of the thermoregulation apparatus is truly remarkable. He points out that, despite the inadequate turning on of thermoregulatory reactions, which at times operate very intensively, significant shifts in the temperature constant often do not set in: The chill-like tremor occurring in diencephalic crises, usually, does not raise body temperature markedly, just as excessive sweating in neuroses does not lower it. The author believes that an inadequate function in one link involves a corresponding restructuring in the system's other links, which protects the temperature constant against disturbance [70]. It should be admitted that neither the very mechanism of such reactions, nor their adaptive significance, nor their starting conditions are clear. It seems that higher regulatory levels and psychophysiological states play a definite role in their performance. As it will be shown below, nor is it ruled out that such curious reactions are encountered in daily life much more frequently than customarily assumed.

3. Terms seemingly borrowed from the field of physiology of energy metabolism, for example, "energy resources of the organism," "energy state," and so forth, are often used in psychophysiology. However, this is an external similarity, because a philosophical or a psychological, not an energy, meaning is invested in them. Furthermore, in the psychophysiological literature these concepts are presented and argued in inadequate units of measurement—such as the cardiac rate, microsiemens or millivolts for electrodermal reactions, and so forth. This approach could be considered symbolic. It should be admitted, however, that this introduces confusion into the interpretation of research results. However, since such designations have arisen spontaneously, consequently it means that the idea of interconnection of psychophysiology with energy exchange has subconsciously occurred to researchers.

In our opinion, the situation that has been created has lowered the prestige of psychophysiology among physiologists and practical medical workers. An unusual situation has arisen. The energy nature of vegetative reactions is trivial. Textbooks and manuals on the physiology of the vegetative nervous system consider the supply of nutrients for tissues and organs, as well as the elimination of final products of energy exchange from the organism, its basic task. Despite this, psychophysiological vegetative reactions, essentially, have not been interpreted from the quantitative positions of energy and heat metabolism.

4. Psychophysiological vegetative reactions are characterized (as noted above) by the lack of their unifying foundation, which explains and forecasts their onset, extinction, and change in an accurately determined order with a certain complex of psychological circumstances and personality characteristics of the individual.

Thus, there are serious difficulties in explaining many fundamentally important cases of the two examined groups of physiological processes (psychophysiological vegetative reactions, on the one hand, and reactions of energy metabolism and physical thermoregulation, on the other). We assume that bringing them closer together will make it possible to give each of them precisely the missing thing that they need. Therefore, during recent years we have tried to formulate the basic principles of interrelations of psychophysiology, on the one hand, and energy and heat metabolism, on the other [2-11].

This work makes an attempt to generalize our ideas of the functional interconnection between psychophysiological reactions and energy metabolism.

TABLE OF CONTENTS

Opioid Peptides—Endogenous Stimulants of Tissue Regeneration

917C0405 Moscow ORTOPEDIYA, TRAVMATOLOGIYA I PROTEZIROVANIYE in Russian No 10, Oct 90 [manuscript received 14 May 90] pp 73-77

[Article by V. D. Slepushkin, Novokuznetsk Branch, Central Institute of Protheses and Prosthesis Design]

UDC 616.71-003.9-07

[Text] The dawn of the science of regeneration belongs to the 1950s and 1960s, when Soviet scientists identified the general patterns associated with the course of regenerative processes in animal bodies and the basic feasibility of controlling the process of regeneration was demonstrated. Experiments that have become classical—those performed by Prof. A. N. Studitskiy in the regeneration of the striated musculature of various representatives of the animal world[45,46]—resulted in the rapid growth of an entire area of plastic surgery[54] and served as the theoretical foundation for the technique of stretching the extremities with Ilizarov's perosseous osteosynthesis.

Because there is a need in practical medicine for regeneration stimulants, pharmacologists have tried and are still trying to create substances that can stimulate the process of regeneration—particularly, reparative regeneration. However, even today, it must be said that physicians simply do not have in their armamentaria effective regeneration stimulants, and preparations such as pyrimidine derivatives have side effects that keep them from being used widely in surgery, traumatology, and opthopedics.

If an endogenous or exogenous substance is to stimulate regeneration, it must have a number of properties that support preliminary processes in the body, the essence of which processes consist of the following: (1) suppression of the stress response, since an excessive amount of catecholamines or glucocorticoids suppresses the regenerative process; (2) support of adequate microcirculation in the area to be regenerated; (3) stimulation of the immune processes; (4) enhancement of energy production in the locus of reparation; and (5) increased synthesis of nucleic acids and nucleus-dependent protein synthesis.[4]

Based on general biological principles, one can speak of the possible presence in the human body and the animal body of endogenous regeneration stimulants, which should exist also in single-cell organisms and should be, in chemical terms, relatively simply structured substances.

In 1975, a new class of biologically active substances were found—enkephalins, which are peptides containing a total of five amino acids.[24] Enkephalins—leucine enkephalins and methionine enkephalins—have been found in all representatives of amphibians, all the way down to the primitive witch-fish [ryba-vedma].[32,52,53] Since enkephalins are ligands of opiate receptors and have a number of morphinelike effects, they have been named opioid peptides. They have been found in virtually all representatives of the animal world, all the way down to single-cell organisms.[55]

One representative of low-molecular peptides that results in the activation of hydra growth has been given the name hydra morphogen. There are 11 amino acids in its structure.[12] The hydra morphogen peptide accelerates the regeneration of organs of coelenterata and polychaeta.[22] Consequently, over the course of evolution, the body formed a system that accelerates differentiation and regeneration of tissue and organs, the products of which are low-molecular peptides, including enkephalins. At the onset of our work, we agreed that regeneration stimulants should effect a number of preliminary processes that ultimately lead to acceleration of regenerative processes. Let us try in that context to analyze the effects of enkephalins.

Researchers have established that the administration of synthetic analogs of enkephalins to stressed animals diminishes in them the activity of the sympathoadrenal system,[9] as a result of which the excretion in the urine of epinepherine, norepinephrine, DOPA, and dopamine is

reduced.[1,2] Enkephalins lower the level of catecholamines in the blood of individuals with acute myocardial infarction[1] and in the adrenal glands of stressed rats.[1]

The exogenous introduction of enkephalins into experimental animals placed in a state of stress lowers the level of CRF secretion in the hypothalamus[15,27] and ACTH in the hypophysis.[15] The glucocorticoid levels of the blood drop.[5,15] In myocardial infarction patients, the administration of the synthetic analog of leu-enkephalin, dalargin, has lowered the content of immunoreactive ACTH and cortisol in blood plasma.[4]

The administration of enkephalins and their synthetic analogs lowers the secretion of vasopressin in rats.[33]

Thus, in supressing the activity of the sympathoadrenal system, the hypothalamic-neurohypophyseal system, and the hypothalamic-neurohypophyseal-adrenal system, enkephalins produce an antistress effect. At the same time, other manifestations of the stress response are also lowered or leveled off: the number of ulcers in the gastrointestinal tract is lowered, and changes in the thyicolymphatic system are less marked.[26] Those data made it possible for us in 1983 to formulate the concept of the enkephalinergic system as an endogenous antistress system,[37,40] which was later confirmed by other researchers.[29,35] We view synthetic enkephalins as promising substances for protecting the body against stress.[38,39]

Consequently, enkephalins satisfy the first conditions, in which substances stimulating regeneration must be able to suppress the stress response.

Some researchers[48,49] have shown that enkephalins stimulate both blood flow and lymph flow in the mesentery vessels of rats. Dalargin improves intraorgan circulation in the pancreas in experimental pancreonecrosis in dogs.[13] Experiments on rats have shown that the collagen-dalargin complex stimulates blood flow in regenerating tissue.[30]

Indirect data based on the dynamics observed in a study of lactate in the blood also indicate that dalargin improves microcirculation in rats with acute myocardial infarction and blood loss[16] and in humans with acute myocardial infarction and obliterative atherosclerosis.[18]

In general, it can be said that enkephalins improve microcirculation, which is an important condition for the stimulation of the regenerative process.[28]

A necessary condition for the realization of the process of regeneration is the stimulation of all the immune components.[3] It has been shown that human and animal lymphocytes have enkephalin receptors.[7,56] The binding of enkephalins by the lymphocytic membrane alters the level of cAMP in lymphocytes, i.e., it has a pronounced physiological effect.[7] The membranes of the cells of the spleen of mice also have enkephalin receptors.[56]

It has been found that lymphocytes and bone marrow cells themselves are capable of synthesizing endogenous opiates called myelopeptides.[56]

Enkephalins have immune-mediating properties. Leu-enkephalin and dalargin stimulate the blastogenesis of cells when their activity is lowered in response to the PHA mitogen, and they inhibit the response of mononuclear cells when the level of donor cell proliferation is initially high.[21] Similar results have been obtained with regard to the lymphocytes of individuals with hypertension,[25] rheumatism, and systemic lupus erythematosus,[8,11] as well as with obliterating diseases of the vessels of the lower extremities.[42]

Consequently, there is no doubt that enkephalins have immune-mediating properties, thereby satisfying the third condition for substances that are regenerative stimulants—effect on immunity.[3]

The next necessary condition for supporting the process of regeneration and reparation of tissue is enhanced energy production.

It has been found that in heart damage in rats caused by administration of large doses of isoproterenol or by ligation of the coronary artery, ATP concentration drops considerably in the myocardium, whereas ADP and AMP levels rise, which leads to a reduction in the energy supply of the adenosine diphosphate system and blockade of energy production.[17,42] Administration of dalargin to rats with hemorrhagic shock prevents a drop in the glycogen levels of the liver.[17] Consequently, enkephalins enhance the processes associated with energy production in damaged organs, thereby supporting reparative processes.

The next necessary requirement for regenerative stimulants is enhancement of the synthesis of nucleic acids and the nuclein-dependent synthesis of protein.[4]

Ornithine decarboxylase is known to be a key enzyme in the processes associated with the synthesis of polyamines. An increase in the activity of that enzyme is observed when there is an increase in the synthesis of protein and nucleic acids in growing tissue.[50] It has been shown that dalargin produces an increase in the activity of ornithine decarboxylase in the mucosal membrane of the duodenum when it is damaged by cysteamine.[50] Dalargin activates the synthesis of DNA and RNA in the mucosa of the stomach and the small intestine.[23] Those findings enable one to clearly assert that enkephalins stimulate the synthesis of nucleic acids and protein in damaged regenerating tissue, which may underlie their stimulating effect on regenerative processes.

The list of literature data cited provides the basis for considering enkephalins as endogenous stimulants of reparative processes, since they satisfy all the requirements for such stimulants.[4]

A certain ratio of intracellular levels of the cyclic nucleotides cAMP and cGMA is known to be a factor determining structural homeostasis. An increase in the intracellular concentration of cAMP in tissue serves as a marker for depression of regeneration, whereas the predominance of cGMA, conversely, signals the activation of the regeneration process.[14,36,51] The ability of enkephalins to lower the content in various tissue of cAMP by depressing the activity of adenylate cyclase has been established.[6,31,43] Direct evidence has been produced for the stimulating effect of enkephalins on regenerative processes. For example, dalargin accelerates considerably the healing of peptic ulcers both in experiment and in the clinic.[10,47] Dalargin is being used successfully in experiment and in the clinic for the treatment of acute pancreatitis[13] and acute toxic damage to the liver by carbon tetrachloride.[34] The findings we have presented on the restoration of organ function, plus the reduced fatality rate among animals given dalargin, point indirectly to the activation of reparative processes.

Enhancement of the regeneration of the epithelium of the stomach and the small intestine by dalargin has been observed in rats in which circulatory insufficiency was being modeled.[22,23]

If the periaqueductal space of the gray matter of the brain is stimulated in rats through implanted electrodes, the healing of skin wounds of the back can be accelerated considerably (by 22 percent), and endogenous opioid peptides take part in the mechanism of that healing.[19] Direct administration of met-enkephalin, leu-enkephalin, or their structural analogs to rats reduces the average healing times for back wounds by 29 - 30 percent. In rats, the administration of dalargin stimulates callus formation in tibia fractures 2 - 3 weeks before such formation in controls.[20,44] It has been demonstrated on a model of organotypical culture of the spinal cord in rats that enkephalins stimulate axon growth and the speed of migration and proliferation of glial and fibroblastlike cells.[21]

Thus, enkephalins produce a stimulating effect on the regeneration of tissue by improving energy production, increasing protein and nucleic acid synthesis, raising the body's immune resistance, and suppressing the stress response.

Since the enkephalinergic system appears in the earliest stages of phylogenesis and ontogenesis,[52,53] it is probable that that system is an endogenous stimulant of the regeneration of tissue in representatives of the animal world.

Apparently, it is possible to use directed synthesis to create enkephalins that would selectively stimulate the regeneration of bones, muscle, and nerve trunks, which would effect a genuine revolution in various fields of medicine, among them orthopedics and traumatology.

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STD Incidence, Treatment Procedures Discussed

917C0011B Moscow RABOCHAYA TRIBUNA in Russian 17 Aug 90 p 4

[Interview with Valeriy Vladimirovich Klyuvayev, dermatologist/venereologist and specialist first-class of the USSR Ministry of Health, by M. Ripinskaya, under the rubric "A Candid Dialogue": "If Venus Has Turned Her Back...": first paragraph is source introduction]

[Text] The current city-dwellers organized a meeting in the current capital region. They wrote irate letters to the Mossovet [Moscow City Soviet]. They circulated leaflets and slogans that said "We will not tolerate infections!" And in Krylatskoye, they demonstrated against the placement of a dermatology/venereology clinic in a new building. V. Klyuvayev, a dermatologist/venereologist and a specialist first-class of the USSR Ministry of Public Health, alluded to that sad fact during our conversation.

Ripinskaya: Valeriy Vladimirovich, wouldn't the goddess of love rejoice, if she found out what terrible ailments had been named after her.

Klyuvayev: "Venereal disease" is an antiquated term that is dying out. According to the World Health Organization classification, grouped with the well-known syphilis, gonorrhea, and trichomoniasis are other diseases that can be transmitted sexually—chlamydiosis, cytomegalovirus infection, viral hepatitis B and, of course, AIDS.

Ripinskaya: On the one hand, the fear of being infected with venereal disease has seemingly diminished. On the other hand, it is fear and ignorance that determine the attitude of many people toward the problems of venereal diseases and their treatment.

Klyuvayev: An example is Krylatskoye. If the inhabitants now only knew that nowadays this is a fallacious argument associated with common syphilis. A clinic in their neighborhood represents no threat whatsoever to them. The way the disease is "acquired" is through sex. And for goodness sakes, everyone is, as the saying goes, the master of his own fate. The statistics are sad: last year, there were many cases of syphilis in Georgia and Moldavia. In the RSFSR, Uzbekistan, Belorussia, and Estonia, the morbidity from gonorrhea exceeds the Union average.

Ripinskaya: Is it a matter of lower morals? A growth in alcoholism? Drug addiction?

Klyuvayev: There's no doubt about that. But some observed that there are outbreaks of infectious diseases in years of an active sun and that they depend on the season. Consider risk groups. There are numerous people without any occupation, bums. That also means uncontrolled contacts. Moreover, venereal diseases have gotten quite a bit "younger". There are many more 14- and 15-year-olds who have gonorrhea or who are having abortions than the physicians and teachers could imagine. From 1985 to the present time, the morbidity rate among children and teenagers has increased threefold. Our children are a great deal different from their postwar counterparts. They are having sexual contact at an early age. You have to admit that prohibitions don't stop lovers from "taking a roll in the hay".

Ripinskaya: And so, God takes care of those who take care of themselves? If you don't want to get a disease, don't have casual sex? For His Majesty Chance rules in love?

Klyuvayev: In the language of venereologists, casual sex is, as a rule, sexual contact with someone you don't know. When future spouses meet, that could also be casual in the beginning. But, after all, you don't get married the next day. That means, you spend some time looking each other over and getting to know the person. And if you suspect that something is wrong, don't delay, go right to the doctor.

Ripinskaya: Then what's confidential will be out in the open. And that's exactly how most people think

Klyuvayev: The doctor in the dermatology/venerology clinic is obliged to examine the sexual partners. That's done all over the world. And it's in the interest of the patient. The fear that it will get reported to where one works and that it will ruin one's career are groundless. The physician is the one who would suffer if he violated confidentiality.

During the past two years, at the initiative of the USSR Ministry of Health, an experiment involving the anonymous examination of venereal disease patients was conducted in Moscow, Tbilisi and Murmansk. Alas, it did not prove itself. It only prepared the ground for postexamination referral of the patients to private-practice physicians (who, at that point, do not bear any responsibility toward the patient), and then to "quacks". Almost every fifth patient failed to make an attempt to find out the results of the analyses and declined any further treatment.

And we didn't have to wait long for the consequences: syphilis morbidity has already increased 1.5-fold in Murmansk, and in Moscow it is roughly three times higher than the Union average.

Ripinskaya: Valeriy Vladimirovich, if I understand you correctly, the time for "wringing one's hands" about venereal disease clinics has passed, but complete democracy in that question is inappropriate. How can that be?

Klyuvayev: It is very difficult to intrude in the purely personal ife of a person. Therefore, most practicing physicians reject the principle of absolute anonymity in examining such patients and propose a new form of monitoring a dangerous infection—coding. A patient is assigned a "code number", say, I-12. Only the treating physician knows the identification card data. The chart is written out for the code number. The patient, if it is necessary, is admitted to the hospital under the code

number. And under that same code number, the infected partner can go to any clinic in the city for help. Nowadays, psychiatrists also assist the venereologists in their work. It is the psychiatrists who try, without injuring the patient's self-esteem, to tactfully question him (confidentiality is maintained) about his sexual partners. Incidentally, the sign "Dermatology/Venereology Clinic" has been replaced in many cities. Now it simply says "Dermatology". I feel that it doesn't pay to keep on emphasizing some particularly indecent meaning of venereal diseases.

Ripinskaya: Perhaps we should think about creating "houses of love" in our country to limit the spread of venereal diseases.

Klyuvayev: It is not necessary to blindly copy the West. From a moral standpoint, that inflicts tremendous harm, especially to our youth. I think that access to public houses would hardly strenthen the family. We wouldn't lower the level of morbidity that way: nowhere near every man who has sex "on the side" would avail himself of such "services". It would more likely be people who have low self-esteem.

Ripinskaya: Valeriy Vladimirovich, and now can you give some advice to those on whom Venus has turned her back. For when trouble has occurred or might occur.

Klyuvayev: At the first sign that something is wrong, go immediately to a doctor. And not to a private doctor (incidentally, the treatment of venereal diseases is prohibited in medical cooperatives), but to a clinic.

If you've had a chance sexual contact, and you have doubts as to whether your partner is healthy, go to the nearest personal prophylaxis point at a clinic within three to five hours (no longer). You will be anonymously given all the necessary examinations there, in order to prevent disease. Personal prophylaxis points will soon be in polyclinics, railroad stations, and at airports.

One should also know about the means available for protecting oneself against venereal disease: condoms, chlorhexidine, and cidipol.

Worsening Diphtheria Situation in Moscow

917C0046A Moscow IZVESTIYA in Russian 6 Sep 90 Morning Edition p 2

[Article by L. Ivchenko "Diphtheria Avenging Lack of Concern"]

[Text] The disregard of diphtheria vaccinations has had sorry results in the country and especially in the capital: this year there were 457 registered cases of diphtheria, 188 of them in Moscow. Ten of the victims died, including three children. The epidemic troubles caused by poorly organized vaccination were the subject of a press conference of the USSR Ministry of Public Health.

Why are many parents trying to protect their children against vaccinations? The head of the Executive Epidemiological Authority of the USSR Ministry of Health, M. Narkevich, like other medical professionals at the press conference, sees the press to blame: ill-considered articles about the complications and even death of children after AKDS (whooping cough, diphtheria, tetanus) vaccinations have caused worried parents to avoid this preventive measure by every means possible. But there are no other ways at present of dealing with certain kinds of infection. Nor is it an accident that the World Health Organization has undertaken an expanded program of immunoprevention: by 1990, every person should have received one vaccination against tuberculosis, one against measles, one against poliomyelitis, and three AKDS. And the "coverage" of the population by vaccination against these diseases should be no lower than 90 percent, or it will not produce the desired effect for society.

But were certain elements of the mass media really wrong in their "tarnishing" of immunoprevention? For doctors themselves also wrote about serious complications after vaccinations. The quality of the vaccines is far from perfect, and children have had convulsions and allergic reactions.

"Complications do happen," agrees Narkevich, "but they are extremely rare, about the same as a traffic accident. Careful examination of all unusual events associated with vaccinations shows that they are caused not by vaccination, but by random diseases coinciding with it. It is not so much a complication, as an unusual, nontypical reaction of the body, in large measure caused by impaired health due to environmental factors. By the way, as medical statistics show, there are 0.2 - 0.6 complications per 100,000 vaccinated children. This is hardly comparable with the threat of tens of thousands dying from epidemics if vaccinations are abandoned."

The following figures speak on behalf of this conclusion. In 1988, 62 of our citizens died of diphtheria, 184 of measles, and 73 of whooping cough. In 1958, i.e., before the massive vaccinations, 4,294 died of diphtheria, 10,125 of measles, and 3,703 of whooping cough. Impressive! According to WHO data, each year 1,350,000 deaths from measles are prevented thanks to immunoprevention. In the Western countries, 96 percent of children are vaccinated. And as a result, last year in the United States there was not a single recorded case of poliomyelitis, and only two of diphtheria. But we had 94 cases of diphtheria in Moscow alone.

And what about other cities? Leningrad is "holding its own", according to Ye. Lakotkina, consultant at the Leningrad Research Institute for Childhood Infections, solely thanks to a well organized vaccination program. For this same reason, there has been no poliomyelitis for many years in the Baltic republics and Byelorussia, and the lowest level of morbidity for diphtheria and other "controllable infections". The highest frequency of measles is in Turkmenia, of poliomyelitis, Azerbaydzhan.

Moscow is currently rivalling the "leaders" in diphtheria: 29 of 33 regions have been affected. There is a very high precentage of vaccination refusals here: more than a third of children under one-year-old are not vaccinated.

The somber situation is now forcing parents to revise their decision. And it is no accident that we, the journalists, have been asked to lend a hand: it is necessary to spread the information, to raise the general medical culture of the population, to advertize the benefits of immunoprevention. It would also be helpful if doctors themselves made an effort, developing vaccination regimes for the weak, those with contraindications, children, organizing vivid information campaigns: there are too few well-written, convincing leaflets, easy to understand posters, brochures. It is also necessary to make the manufacturers of the vaccines bear full responsibility for their quality.

"All costs for production of a drug that departs from the strict standard should be laid to the account of the guilty parties, not just depriving them of the production bonus," says the director of the Executive Authority for Protection of Motherhood and Childhood of the USSR Ministry of Health, I. Leshkevich. "Perhaps then there will be greater zeal and more quality supervision."

Diphtheria Situation in Ukraine

917C0046B Kiev PRAVDA UKRAINY in Russian 28 Sep 90 p 4

[Interview with V. F. Mariyevskiy, head of the Executive Sanitary- Epidemiological Authority of the Ukrainian SSR Ministry of Health, "Is Diphtheria Returning?"]

[Text] As already reported in the press, an increase in the cases of diphtheria has been noticed in Moscow. Are we not also faced with a similar problem? What measures should be taken in the Ukraine? These questions were discussed at a conference at the sanitary epidemiological station of the republic. Professor and epidemiologist K. M. Sinyak, chief pediatrician of the Ukrainian SSR Ministry of Health V. V. Berezhnoy, professor O. N. Kostyukovskaya, Ye. A. Shablovskaya, A. V. Tyazhkaya, and other specialists expressed their views and opinions. Medical commentator of PRAVDA UKRAINY, Yu. Vilenskiy, paid a visit to V. F. Mariyevskiy, head of the Executive Sanitary-Epidemiological Authority of the Ukrainian SSR Ministry of Health.

"In the Ukraine, cases of diphtheria have been reported in 19 oblasts, Kiev, and Sevastopol," said Mariyevskiy. "But this does not mean that a sudden outbreak of the infection has occurred. A trend to a certain increase in the number of cases has been noticed over the past ten years. Thus, in 1989, there were 59 recorded cases of diphtheria in the republic. But given the fact that 219 persons fell ill in Moscow, including 43 infants, the situation must be viewed as serious."

Question: You know that, in the past, there was an active campaign of immunization against diphtheria. This tactic caused the infection to recede. What is the situation at present?

Answer: Unfortunately, this preventive system is weakened today. Studies have shown that around 40 percent of children are not protected against diphtheria by immune means. And the fewer number of people with secure immunity against a particular infection improves the chances for its spread, for the laws of epidemiology are unshakeable. It is very alarming that immunity against diphtheria is lacking in many adolescents aged 14 - 16 years. There is also disease among adults. Parents often refuse vaccinations, evidently not realizing that it is very dangerous to leave children unprotected against possible encounter with diphtheria infection. Unfortunately, the press has also helped foster a negative attitude toward immunization, even though the journalists also had just cause. But as you can see, there is no joking with diphtheria. Let me emphasize that only 3 percent of children have actual contraindications for vaccinations. Moreover, the techniques of vaccination are being steadily improved. Finally, we cannot expect a favorable outcome in abandoning vaccination.

Question: The sanitary epidemiological service is now working toward a specific campaign of prevention and is prepared to combat diphtheria. But what is the role of other specialists?

Answer: We are counting on an active position of pediatricians, consistently explaining to the population how important a defensive policy against diphtheria is today. Ensuring that virtually every child is immunized remains an important measure, and we will promote this in every way, since certain organizational problems still exist. Let me mention that a revaccination of adolescents is being done at the age of 14 - 15, instead of the previous regulation at age 16. There is no need to demonstrate how urgent this is.

The diagnostic vigilance of otolaryngologists should also be heightened, since diphtheria is often confused with angina. Timely examination of the patient by a specialist will clarify the picture. And in conclusion, I would like to urge people once again to reconsider their attitude toward vaccinations. These measures are still vitally important. It should be pointed out, in particular, that the maximum number of throwaway syringes are being made available by the Ukrainian SSR Ministry of Health and other organizations for vaccination. And it is also necessary to caution people: do not treat angina by yourself. It may be that diphtheria is lurking beneath its mask, and only a doctor can establish this and organize proper treatment.

Economic Relations in Activity of Therapeutic and Prophylactic Institutions Under Conditions of New Economic Mechanism

917C0080A Moscow SOVETSKOYE ZDRAVOOKHRANENIYE in Russian No 7, Jul 90 pp 3-5

[Article by V. A. Minyayev, N. I. Vishnyakov, N. V. Trofimova et al.; 1st Leningrad Medical Institute imeni I. P. Pavlov; Territorial Medical Association No 19, Leningrad]

UDC 614.2(470.23-25)

[Abstract] An experiment on reconstructing the public health system in Leningrad has entered its second year. The essence of the experiment took into consideration the fact that economic levers are being introduced into the public health system and these levers make it possible for public health agencies to seek internal reserves actively and to spend capital most rationally so as to improve the quality of medical care. The reconstruction has made it possible to pay physicians and nurses according to the final result which improves medical care and morale of the medical workers. Realization of the economic experiment involved organization of territorial medical associations, including different medical institutions, basically of the out-patient-polyclinic type. These associations have become the main health care provider but specialized types of medical assistance come from other hospitals on a contract basis. There has been a decrease in unnecessary hospitalization and an increase in planned hospitalization. Intensification of labor has permitted a considerable increase in wages. The intrasectoral cost accounting relationships have proved to be a progressive form of public health organization and management.

Parturient Women From Other Cities in Moscow

917C0080B Moscow SOVETSKOYE ZDRAVOOKHRANENIYE in Russian No 7, Jul 90 pp 28-31

[Article by Ye. L. Dubinskaya, All-Union Scientific Institute of Social Hygiene, Economics and Public Health Administration imeni N. A. Semashko, USSR Ministry of Health, Moscow]

UDC 614.1:312.1-054.68(470.311-25)

[Abstract] Latest data indicated that more than 10 percent (13,000) of parturient women treated in one year in Moscow are from other cities. This situation resulted from poor organization of assistance in births in some regions. Statistical analysis of the "geography" of arrival of women from other cities to give birth in Moscow made it possible to single out regions in which care of expectant and parturient mothers should be improved. Most of the women (75 percent) came to Moscow from Moscow Oblast and 60 percent of these came from nearby regions. Many came from Georgia SSR, Azerbaijan SSR and the RSFSR. There was a high correlation between the number of women coming to Moscow for birthing assistance and the educational level of women in republics from which they came. The relative intensity of frequency of women coming from other cities in different regions of the RSFSR was tabulated and discussed.

Treatment-and-Prevention Facilities and the Economic Mechanism: New Conditions, New Problems

917C0081 Moscow ZDRAVOOKHRANENIYE ROSSIYSKOY FEDERATSII in Russian No 7, Jul 90 pp 3-6

[Article by V. I. Starodubov, RSFSR Ministry of Health]

UDC 614.2:008

[Text] The many years of development of our health care system in a setting in which the work of the medical facilities was evaluated primarily by means of quantitative indices (number of beds, doctors, mid-level medical personnel, bed-days, visits, etc.) resulted in very low quality in terms of the medical care that was given to the population. That is why the medical profession showed great interest in the new economic mechanism that began to be implemented in 1988 in Leningrad, as well as in the Kemerovo and Kuybyshev oblasts.

To a large extent, the negative processes in the country's economy are also reflected in the development of health care—one of the most critical components of the social sphere. And it is unrealistic to hope for a radical change in the financing of our sector in the near future. Still, it must be said that the budget of the Russian Federation health care sector rose to 12.47 billion rubles (R) in 1989 from R9.94 billion in 1987.

The social impatience of society with regard to the deficiencies in the provision of medical care requires that health care organizers and physicians produce a real improvement of the situation in health care, notwithstanding inadequate financing and in the shortest possible time.

The experiment that was carried out was based on the introduction of an economic mechanism and the establishment of proper criteria for evaluation of the activity of the medical workforce under conditions of greater independence.

Demographic data and indices characterizing the activity of the health care facilities of Leningrad, the Kemerovo and Kuybyshev oblasts, and the RSFSR in 1987 - 1989 are presented in the table. That time interval was chosen on the following grounds: 1987 is the base year, prior to the experiment; 1988 is the period of transition to new economic conditions in the three territories; 1989 represents the operation of the treatment-and-prevention facilities in relatively stable relationships under the conditions of the new economic mechanism.

Demographic data and indices of activity of the health care facilities of Leningrad, the Kemerovo and Kuybyshev oblasts, and the RSFSR in 1987-1989

Index	Leningrad			Kemerovo Oblast			Kuybyshev Oblast			RSFSR		
	1987	1988	1989	1987	1988	1989	1987	1988	1989	1987	1988	1989
Total mortality (per 1000 persons)	11.7	11.6	11.6	9.9	10.3	10.5	10.3	10.5	10.5	10.5	10.7	10.7
Infant mortality (per 1000 live births)	18.0	19.0	17.1	19.5	20.7	20.1	19.1	18.5	17.4	19.4	18.9	17.7
Maternal mortality in medical hospitals (per 10,000 births)	1.9	2.6	2.7	2.4	2.8	3.9	2.2	3.6	2.8	2.9	3.1	3.4
Tuberculosis morbidity (per 100,000)	25.5	24.5	21.8	44.9	41.4	38.0	37.7	35.5	34.0	42.4	40.6	36.9
First-time identified drug or toxic substance abusers (per 100,000)	13.8	10.0	5.6	8.9	5.4	5.5	13.0	8.0	4.6	8.0	5.6	4.9
First-time identified alcoholics (per 100,000)	157.0	173.7	161.9	249.0	225.1	198.0	206.6	211.6	179.7	218.0	192.6	163.6
First-time diagnosed cases of syphilis (per 100,000)	10.1	7.6	7.7	2.0	1.2	1.2	4.9	5.8	4.2	5.1	4.3	4.2
First-time diagnosed cases of gonorrhea (per 100,000)	210.3	224.1	255.2	129.3	132.8	154.9	113.2	121.3	154.3	115.7	113.6	134.0
First-time diagnosed malignant tumors (per 100,000)	322.0	316.6	323.2	238.6	250.6	236.9	283.1	286.6	284.1	259.9	263.0	240.9
Number of abortions per 1000 women aged 15-49	107.2	105.8	99.7	131.7	116.4	96.3	113.4	105.9	101.2	113.6	104.2	106.0
Number of blue-collar and white-collar workers (per 10,000) declared disabled for the first time	61.9	59.8	50.6	37.4	36.9	38.6	68.7	52.6	48.2	48.1	46.7	45.8
Temporary disability among blue-collar and white-collar workers (per 100), in days	1303.1	1258.0	1225.9	894.0	958.9	1021.0	844.7	888.7	940.2	894.3	939.6	942.7
Average hospital stay, in days	17.0	16.6	16.9	15.9	15.7	15.6	15.3	14.7	14.4	16.3	16.0	16.2
Number of hospital admissions (per 100 persons)	20.6	20.4	19.7	28.8	27.9	25.9	25.8	24.8	24.0	25.1	24.9	23.6
Average number of days of bed occupancy per year	306.2	292.1	282.8	326.1	314.8	313.2	322.9	300.1	295.5	316.4	307.3	295.0

As is evident from the table, the changes in almost all the indices of the three territories conform to the trends characteristic of the RSFSR as a whole. One notes a decrease in infant mortality and morbidity associated with tuberculosis, chronic alcoholism, and syphilis, as well as a rise in maternal mortality and in morbidity with temporary disability.

In light of the qualitative indices for the operation of the health care facilities of the three territories, one must admit that the new economic conditions are not a panacea for all the ills of health care.

The switch from itemized financing to normative financing enables a fairer allocation of the budget. In addition to state budget allocations, treatment-and-prevention facilities can now have extrabudgetary sources of income by negotiating contracts with enterprises and expanding the paid services they offer to the population. The rights of the health care facilities and their independence in the selection of an economic model and their right to choose the organization of labor and wage forms have been enlarged considerably. It is now possible to differentiate the wages of each employee according to the quality of his work.

The initial results of the operation of the territories under the new conditions show that there has been an elimination of the mid-level management components (the rayon health departments and most of the municipal health departments have been abolished). Territorial medical associations (TMO) have been created. The optimal structure of the TMO is one in which a single association integrates the pediatric, internal medicine, obstetric, and other basic kinds of polyclinic services for the adult and child population. That makes it possible to shuffle staff and to create obstetric/internal medicine/pediatric work teams.

The transfer of basic monetary funds to the polyclinics on the basis of norms per inhabitant and the use of those funds to pay for the services of other facilities has justified itself in principle. That measure becomes especially effective in conjunction with the collective work contract. Such a contract expands considerably the rights of the facility's employees, including the director. It mobilizes the entire staff to intensify labor, improve its quality, and exercise a prudent regard for material resources. Most effective in that respect have been economic levers, especially material labor incentives. With the collective work contract, the labor of each employee is remunerated by decision of the work force, in view of the results he produces. It should be mentioned that the quality indices of the work of the facilities are improving in TMOs in which economic incentives have been adopted, and progressive forms of service to the population are being introduced in a vigorous fashion.

Improvement of the quality of primary medical care is still being held back by the following factors: a weak material-technical base for the polyclinics and outpatient clinics, inadequate stocks of medical equipment, and lower skill levels among the physicians at the outpatient clinic/polyclinic level than among those at the hospital level. Understandably, such problems cannot be solved in 1 ½ - 2 years, but it should be noted that the leading position of the polyclinic in the new economic mechanism has determined the positive trends in the solution of those problems.

Distinct patterns have been noted in the work of the hospitals (see table). The waiting lines for hospital admission have been virtually eliminated. The bed fund has been reduced by cutting back on unwarranted hospital admissions and reducing the length of bed stay per patient by means of improving the operation of the polyclinics and intensifying the treatment process in the hospitals.

Furthermore, the development of new forms of operation (daytime hospitals at the polyclinics, day hospitals, and home care) is also helping to reduce the bed fund, and there are substantial reserves in that area.

For example, in the Kuybyshev Oblast in 1989, a total of 10,815 patients were treated at the daytime facilities of the hospitals, 20,238 were treated at the daytime hospitals of the polyclinics, and 9,141 were treated in the home care program. Those patients underwent complete courses of medical treatment lasting an average of 10 - 15 days.

Providing the labor force and individual workers with an economic stake, in the end the results of the work is impossible without a clear definition of the concept of end result and without the creation of a method of measuring the degree of its achievement. In the territories, systems of medical-care quality control have been created on the basis of the standards that, on the one hand, enable monitoring of the work of the outpatient and polyclinic facilities and the TMO as a whole; on the other hand, the criteria underlying the statistical groups of the clinics establish clear requirements that the polyclinics may impose on the hospitals.

If the quality standards are violated, economic penalties are used against the perpetrator. The use of a rigorous mechanism which links the quality and volume of activity with the size of the economic incentive has been one of the critical factors preventing serious negative effects that could inflict harm on the patients.

The introduction of specialized services in the new economic mechanism remains a complicated question. The territories have used two variations: "horizontal", when the specialized services are part of the TMO; and "vertical", when oblast and interrayon associations such as "Ftiziatriya" [Phthisiatry], "Narkologiya" [Drug Abuse Study], and "Stomatologiya" [Stomatology] are created and financed from central sources. Each variant has its pluses and minuses. Even so, at the initial stage of adoption of the new economic mechanism, preference must be given to the "vertical" variation, which allows the specialized health care facilities to keep their role.

In mentioning the positive aspects of the new economic mechanism, at the same time we must note that its introduction is encountering great difficulties and bringing up puzzling questions.

Chief among them is the financing by norm per inhabitant. The current situation in the economy of the republic does not give promise of an appreciable increase in health care allocations, and the current norm reflects the capability of the budget, not what the sector needs in terms of funds to provide medical care to the population. Yet, funds from the industrial enterprises and organizations and from the population in return for additional services cannot be acquired because of the lack of legislative and normative acts.

The adoption of the new mechanism is being hindered by the flaws in the system of repayment for treatment of patients in hospitals on the basis of the clinical statistical groups (KSG) that have been worked out. And here, too, a sensible system for price setting is being blocked by our budget financing capabilities.

The lack of legislation with regard to the new economic mechanism is making it hard to bring departmental medicine into mutual funding relationships, and it is hindering payment in third-party joinders brought against enterprises and individual citizens by health care agencies and facilities for injury caused to the health of the population.

The adoption of mutual financial relationships among health care facilities and the adoption of mutual accounts within facilities will inevitably lead to a substantial increase in paperwork, and the only way to solve that problem is to computerize our hospitals and polyclinics.

Many problems are associated with the introduction of the new economic mechanism, but the primary problem confronting health care organizers is the moral and psychological preparation of the medical workers to accept it and work in a new way.

In territories where competent and enterprising health care managers have solved that problem and have succeeded in creating labor collectives of like-minded individuals at the polyclinics and hospitals, the quality of medical care provided to the population has risen considerably. As an example, we can mention TMO No. 19, the Sestoretskoye RTMO (Leningrad), the Kinel-Cherkasskoye TMO and TMO No. 10 (Kuybyshev Oblast), and the Tissulskoye RTMO and oblast ophthalmological hospital (Kemerovo Oblast).

It must be pointed out that there is no chance of a return to the old ways in such medical work forces.

The health care sector of Leningrad and of the Kemerovo and Kuybyshev oblasts is not standing still. Its organizers are quickly solving the problems which arise in the course of adoption of the new economic mechanism and are seeking additional ways of improving it. In connection with the transition of a number of territories to regional cost accounting, the role of the local soviets in protecting the health of the population is being greatly enhanced. It is necessary to find and develop levers of economic influence on the enterprises and to create a stake for them in preserving the health of their own employees and the entire population. The solution to this problem is seen as a change to a state-run insurance system to finance the health care process.

The population and the medical workers have justifiable reservations that the health of the patient in the new economic mechanism will not be protected either economically or by legal principles. Furthermore, not even a healthy individual is able to recoup the funds he pays out in the form of taxes and various fees for his own recovery or rehabilitation. The only way to solve such problems is to develop and adopt a law involving a system of medical insurance for the population of the USSR.

In conclusion, it should be mentioned that a radical change in the management of health care is contemplated by ensuring real independence of the staff of the treatment-and-prevention facilities in terms of choosing the best ways to achieve the goals placed before them. The new economic mechanism helps mobilize the reserves existing within the sector and can serve as a stage in the transition toward a new system of organization of the country's health care.

Optimization of Hospital-Based Pediatric Ophthalmologic Services in Ukraine

917C0229A Odessa OFTALMOLOGICHESKIY ZHURNAL in Russian No 3, 90 (manuscript received 29 Dec 89) pp 133-136

[Article by N. F. Bobrova, V. I. Levtyukh, Ye. I. Anina and N. N. Bushuyeva, senior scientific fellows, Odessa Order of the Red Banner of Labor Scientific Research Institute of Eye Diseases and Tissue Therapy imeni Academician V. P. Filatov]

UDC 617.7-053.2-082(477)

[Abstract] Statistics reveal impressive gains in pediatric opthalmologic services in the Ukraine in the 1975 - 1988 timeframe, consisting of a 1.7-fold increase in assigned hospital beds from 930 to 1,610, and a 2.5-fold increase in specialized departments dedicated to pediatric eye care (from 14 to 35). Concomitantly, however, the patient load increased from 12,600 to 38,700, or 3.1-fold, and the number of surgical procedures increased from 8,000 to 15,400, or almost 2-fold. Between 1947 and 1989 the incidence of inflammatory eye diseases fell from 45.7 to 7.5 percent of the total morbidity spectrum, trauma and its consequences remained virtually unchanged in going from 23.1 to 26.1 percent, congenital eye diseases showed an increase from 23.1 to 32.1 percent, the incidence of neoplasms rose from 5.3 to 10.8 percent, and oculomotor disorders from 2.2 to 23.5 percent. In general, two-thirds of the children seen at the Filatov Institute are from the Ukraine, and the number of cases requiring microsurgery has risen from 80.6 to 87.4 percent between 1985 - 1989. One of the most serious health problems consists of penetrating ocular trauma complicated by the fact that emergency surgical care is all too often inadequate, requiring corrective follow-up surgery at specialized institutions. Analysis of the morbidity patterns indicates quite clearly that further developments in Ukrainian pediatric ophthalmology will have to concentrate on improving ocular microsurgery at the primary care level and in expanding eye tumor services. Tables 3; references 10: Russian.

Use of Hybrid Scanner as Counter of Radiation From Man

907C0857 Moscow MEDITSINSKAYA RADIOLOGIYA in Russian Vol 35 No 6, Jun 90 pp 27-29

[Article by A. B. Luchkov and V. I. Trushin; MNIRRI; Ministry of Health; RSFSR]

UDC 615.47.03:615.849.1.015.3

[Abstract] Prospects of the use of "hybrid scanner" devices in radionuclide diagnostics have been quite favorable. The All-Union Scientific Research Institute of Instrument Making has developed this type of device, the radiocorpograph RIK-01, which is now in the testing stage. A method of monitoring mixtures of ^{137}Cs and ^{134}Cs in the body of a patient has been achieved on the prototype of this device, "SKANIKAMERE", developed in France. The scanner has a small methodological error of +/- 3 percent for a nuclide uniformly distributed in a patient's body. The minimal detectable activity for this type of device was 40 nCi. The RIK-01 can produce comparable results. The "SKANIKAMERE" was used to examine more than 340 patients who participated in the Chernobyl Atomic Power Plant accident clean-up or who lived in the territory affected. A formula was derived which may be used to optimize the entire process of measurements for counting radiation incorporation in a person. It was used to find optimum sizes of the slot collimator of the device. A diagram of the detector part of the "hybrid scanner" was presented and described. Figures 1; references 1.

Concentration of Plutonium in Environment and in Human Body

907C0863 Minsk ZDRAVOOKHRANENIYE BELORUSSII in Russian No 6, Jun 90 pp 35-38

[V. G. Mikhalchenko; Belorussian Scientific Research Institute of Hereditary and Congenital Diseases]

UDC 614.73:614.876

[Abstract] Data from the literature provided information concerning amounts and specific features of pollution of the biosphere by global fallout of plutonium. Information concerning fallouts from the Chernobyl accident showed that it led to emission into the environment of plutonium-239 and other alpha-active nuclides including ^{241}Am, ^{242}Cm and ^{244}Cm. Plutonium concentration beyond the 30-kilometer zone and near the zone of the Chernobyl accident was discussed. Fallout reaching Austria and Japan, Germany and other countries was discussed. Soil pollution caused by the fallout, migration in the biosphere and ingestion in food were discussed. Physico-chemical properties of plutonium determined its low migration capacity and insignificant ingestion of food. Maximum permissible annual ingestion of plutonium was discussed. Models of plutonium metabolism confirmed the scientific data. Deposition of plutonium in the organism and its excretion from the body was discussed. The effect of milk in the diet was discussed. The calculated doses of plutonium from Chernobyl incorporated into the organs and tissues for the general population was less than that from natural sources. References 25: 14 Russian, 11 Western.

Effect of Small Doses of Ionizing Radiation on Human Health

917C0065A Kiev VRACHEBNOYE DELO in Russian No 7, Jul 90 pp 79- 82

[Article by A. N. Kovalenko, Institute of Clinical Radiology of the All Union Science Center for Radiation Medicine of the USSR Academy of Medical Sciences, Kiev, with the footnote "published for purposes of discussion".]

UDC 613.116

[Text] One of the conceptual understandings of radiobiology is that the overall damaging effect of low doses of ionizing radiation produced by its direct and indirect action is so slight that it is repaired on the same (cellular molecular) level on which it arises. In other words, the radiation factor eliciting primary physico-chemical processes in the tissues does not entail a subsequent centrifugal phase of reactions. In this it is fundamentally different from the natural factors of physical and chemical kinds that are characterized by response reactions on higher levels.

Yet observations have established that the processes which occur in highly organized biological subjects under external relatively uniform exposure to low doses of radiation may be more complex in terms of succession and interdependence. From the injured tissues, signals as to the resulting damage are sent to the central regulatory systems, whose functional elements are at the same time exposed to the identical influence. Therefore, a dual influence is exerted on the "center"—the central nervous system (CNS), the autonomous nervous system (ANS), and the endocrine system. The analytical and synthetical functions of the neuro-endocrine regulatory systems and the interaction among them are disturbed. A condition develops that may be characterized as a disintegration syndrome, the outcome of which is a sharp decline of the mechanisms of compensation and adaptation. First and foremost, there are disruptions in the regulation of the vegetative tonus. Clinically, this is manifested by a preponderance of the sympathetic or parasympathetic division of the ANS. A periodic predominance of now one, then the other, is possible.

Meanwhile, the body like any other self-regulating system with a large strength reserve continues to struggle and maintain the basic homeostatic characteristics within the range of normal fluctuations, but is not always successful. For example, in certain persons who took part in the cleanup of the aftermath of the accident at the Chernobyl nuclear power plant, significant changes in

the leucocyte formula and a reduced quantity of leucocytes, lymphocytes and thrombocytes, or vice versa, were observed after leaving the 30-kilometer zone. This testifies to the lack of balance in the functioning of the systems that regulate hemopoesis. The compensation processes gradually intensify and the injuries resulting from direct (specific) contact of ionizing radiation with molecular and cellular structures on all hierarchical levels of the body are restored. There is also an indirect (nonspecific) action in the form of a higher level and excess accumulation of peroxide compounds and other radiotoxins. This complicates the course of the restorative processes, thus bringing about the formation of the ultimate radiobiological effect.

Obviously, the processes of restoration and compensation take place more quickly in those tissues whose cells have a high index of self-renewal (mitotic index). These are the cells of the blood-forming bone marrow, spleen, intestinal epithelium, and others. Such processes occur more slowly in cellular associations with low self-renewal, especially in highly differentiated postmitotic cells of the nervous and muscular systems.

If the damaging effect does not ultimately surpass the protective capacities of the body and exceed the strength reserve (or threshold), total elimination of all radiogenic effects will ensue. Moreover, if the exertion of the protective forces to compensate for and eliminate slight, but simultaneously arising injuries in all the organs and systems does not cease, but is prolonged and becomes a kind of hypercompensation factor, then the weak damaging influence of low doses of ionizing radiation is transformed into a biostimulatory effect. Essentially, this cannot be positive, since the biostimulatory or "homeopathic" influence of low doses of ionizing radiation involves a shifting of the "vector of organic economy" in the direction of a decrease. In other words, the body increases its potencies not because of its own growth program, but because of external instigation, or artificial stimulation.

Another situation is quite feasible, when the damaging effect is beyond the threshold of stability, for example, as a result of: a) genotypic or phenotypic predisposition, as is observed in certain members of the human population (in typological respect the population is heterogeneous); b) previous exposure of the body to risk factors of nonradiation nature, against the background of which the ionizing radiation has a releasing or triggering action; c) already existing incipient disease conditions and pathological changes in the organs and tissues, resulting in a heightened susceptibility.

We should not overlook the possibility of a synergic action of a complex of factors, including stress. The adverse influence of these was observed during the accident at the Chernobyl nuclear power plant and its cleanup. In these cases, the injuries resulting from exposure to low doses of ionizing radiation are not completely compensated. While the primary (direct and indirect) radiation effects may be eliminated on the cellular-molecular level, this does not mean that the regulatory systems can return to normal functioning after disregulation, and that an adequate (in qualitative and quantitative respect) arrival of information along the vertical direction ("top to bottom" and "bottom to top") is preserved. That is, the feedforward and feedback between the central information-regulatory and peripheral effector systems of the body are not restored to full extent.

In the situation that we are discussing, the disintegration (disregulation, disadaptation) syndrome is preserved in more or less reduced form. This provides fertile soil for development of relatively persistent functional disorders, which are nothing less than prenosological (incipient disease) states, or for a transition of these to a pathology. Pathological processes may be aggravated, assuming a more severe and torpid course. Disintegration syndrome of larger or smaller extent is essentially a condition that is clinically defined as a syndrome of vegatative dysfunction, with its common symptoms—vegetative-vascular dystonia (VVD), neurocirculatory dystonia (NCD), and a complex of asthenic symptoms. This should be termed *nonspecific radiation syndrome.* It arises after short term exposure to doses of ionizing radiation which do not produce acute radiation sickness (ARS). After overcoming ARS, which is the specific radiation syndrome, the symptoms of nonspecific radiation damage come into the forefront. The disturbances of the integrative activity of the central vegetative structures of the nervous system and distortions of the information flow are inadequate, paradoxal reactions of the physiological systems of the body to the many stimuli and functional tests that are exciting the vegetative and mediatory systems of the brain.

Thus, in certain members of the human population there is found a greater radiosusceptibility, due to typological predisposition, and this is worthy of special investigation. Congenital individual genotypic and phenotypic peculiarities of the vegetative tonus ultimately determine the major clinical symptomatology. There are pronounced sympatho-adrenal, vagoinsular, and combination types, as well as transitions among them. In accordance with this, the nonspecific radiation syndrome will exhibit a predominance of sympathetic or parasympathetic tonus of the ANS; in the combination or transitional types, there will be a parallel or consecutive (periodic) manifestation of either one. Previous premorbid states and pathological processes, as an echo of previously occurring exogenic and endogenic risk factors, create a favorable pathogenetic background for subsequent realization of somatic effects in nonspecific radiation syndrome.

The mechanism of the biological action of psychoemotional stress, in its nature and the sequence of events, is largely opposite to the influence of ionizing radiation on the body. Nevertheless, the stress influence of ionizing radiation, which many perceive as a real threat to health, eliciting additional asthenization and

pseudoneurotic reactions and weakening the integrating role of the CNS and the higher regulatory centers of the ANS, helps fortify and close the vicious circle in the formation of nonspecific radiation syndrome, greatly complicating its clinical course.

Thus, in defining the concept of "vegetative dysfunction" and creating a classification of this for purposes of radiation medicine, we must consider the following: first, the nonspecificity of disintegration syndrome (or vegetative dysfunction syndrome), which is often observed after exposure to doses of radiation not causing ARS, accounts for the absence of the well-known "cause-effect" relationship. The latter comes about only in the dose range producing specific changes in the organs and tissues, in particular, the bone-brain syndrome. At lower doses, this relationship "doesn't work", for this is a qualitatively different level of interaction of the body with the damaging factor, which may be termed an ultrainteraction. Secondly, nonspecific radiation (disintegration) syndrome is the consequence of primary radiation injuries and secondary radiation disorders of the functional activity of nonrenewable, highly differentiated cellular systems, which are responsible for the perception, processing of information, and subsequent regulation of critical vegetative and homeostatic functions of the body. Thirdly, there is no need for an artificial division of the full diversity of clinical manifestations of nonspecific radiation syndrome into separate clinical forms, such as VVD, NCD, and asthenic states. It is a question of pathogenetically identical disturbances in the information-regulatory sphere, the external clinical manifestation of which is psychological and vegetative instability.

In order to emphasize the primary (initiating) role of the radiation factor in the formation of vegetative dystonia syndrome, regardless of its clinical picture, we propose that the latter be defined as nonspecific radiation syndrome. In this way, we distinguish it from other neurovegetative and psycho-emotional disorders that are primarily caused by other exogenic and endogenic factors, or which arise secondarily against the background of existing somatic and neurological illnesses.

Unfortunately, the clinical manifestations of nonspecific radiation syndrome are not confined to the basic forms: VVD, NCD, astheno-vegetative states. The traditional use of these diagnoses alone greatly impoverishes the panoply of clinical manifestations of generalized nonspecific radiation syndrome that will be encountered by the specialist in radiation medicine or occupational diseases.

Radiation medicine is an interdisciplinary science, for the influence of ionizing radiation is universal. Therefore, all processes and changes in the body exposed to radiation, whatever the dose burden, must be considered as a whole, or else the matter will be reduced to questions of a particular pathology. The lack of an integrated understanding of low radiation effects will again lead, in the final analysis, to a rejection of the modifying influence of low doses of ionizing radiation on human health and greatly reduce the effectiveness of therapeutic and preventive measures.

Estimates of Patient and Medical Personnel Exposure in Accidents at Gamma-Irradiation Suites

917C0219A Moscow MEDITSINSKAYA RADIOLOGIYA in Russian No 11, Nov 90 (manuscript received 19 Feb 90) pp 35-37

[Article by R. B. Likhovetskaya, T. G. Ratner, A. I. Sevastyanov and L. A. Maryina, All-Union Oncological Scientific Center, USSR Academy of Sciences, Moscow]

UDC 614.876-02:615.849.114.065+616-001.28-057-02:614.876-02:615.849.114

[Abstract] Estimates were conducted on possible exposure levels sustained by medical personnel during emergency evacuation of patients from gamma-irradiation suites. Dosimetric studies conducted at AGAT-S, AGAT-V and Selektron cobalt bomb suites and determination of the most likely movement patterns showed that the radiology personnel were likely to sustain exposures of 4 - 5, 1 - 1.5 and 0.2 - 0.3 mSv, respectively. Actual exposures would depend on actual movements and response times and activities of gamma radiation sources. Charts relating distance from source to estimated dose level should be posted in radiology suites for safety reasons. Figures 3; references 3: Russian.

Radionuclide-Labeled Liposomal Probes for Malignancies

917C0219B Moscow MEDITSINSKAYA RADIOLOGIYA in Russian No 11, Nov 90 (manuscript received 15 Nov 89) pp 44-47

[Article by N. A. Kostenikov, N. P. Fadeyev and O. A. Rozenberg, Central Scientific Research Radiodiagnosis Institute, USSR Ministry of Health, Leningrad]

UDC 616.006.04-073.916-059:[615.451.234:577.352.2

[Abstract] A survey of largely Western literature is presented on the use of radiolabeled liposomes in the practice of oncology. Recent developments have shown the utility of ^{111}I, ^{67}Ga and ^{99m}Tc as labels for liposomes designated for cancer diagnosis. Animal trials have shown that targeting of malignancies is improved by nonspecific blockage of the reticuloendothelial system. In addition, even in the absence of such blockage, delivery to tumors is often improved by using liposomes bearing a negative charge. The latter was attained by incorporating negatively charged glycolipids, such as

monosialoglycosides or phosphatidylinositol. In addition, liposomes can also be specifically targeted by covalent conjugation of monoclonal antibodies. In addition to diagnostic utility, liposomes have also been studied for their therapeutic potential in delivering radionuclides or antineoplastics to selected sites. References 78: 18 Russian, 60 Western.

Pathological Anatomy of HIV-Infection According to Data of Serologically Verified Observations

917C0068A Moscow ARKHIV PATOLOGII in Russian Vol 52 No 7, Jul 90 pp 9-16

[Article by A. P. Avtsyn, Yu. G. Parkhomenko, A. A. Zhavoronkov et al.; Scientific Research Institute of Human Morphology; USSR Academy of Medical Sciences]

UDC 616.98:578.828.6-06-036.88-07

[Abstract] Observations of four persons who died of serologically confirmed HIV-infection in the USSR included: a case of HIV-infection complicated by a generalized form of Kaposi's sarcoma, a case complicated by pneumocystis carinii and candidiosis pneumonia, a case involving a patient with second stage of syphilis against a background of rheumatism and a case involving a generalized form of lymphoadenopathy. The patients were young males, two of whom came from African countries in which AIDS is endemic. Each case was described in some detail. The disease arose against a background of previous pathological processes which affected the pathological picture in some manner. All patients displayed morphological signs of immunodeficiency involving some degree of atrophy of lymphoid tissue. All patients were promiscuous; one was a homosexual. Figures 4; references 9: 5 Russian, 4 Western.

Concerning Interaction Between Cytomegalovirus Infection and Immunodeficiency

917C0068B Moscow ARKHIV PATOLOGII in Russian Vol 52 No 7 Jul 90 pp 16-20

[Article by V. A. Tsinzerling, G. G. Vasilyeva, M. G. Indikova and S. D. Popov; Central Scientific Research Laboratory (head-Doctor of Medical Sciences V. A. Tsinzerling); Leningrad Pediatric Medical Institute, Children's Municipal Hospital No 1; Leningrad; Kalmuk ASSR Republican Hospital]

UDC 616.98:578.828.6]-06:616.98:578.825.12

[Abstract] Study and analysis of autopsy reports of 87 cases of cytomegalovirus infection included consideration of 66 cases reported in Elista in 1984 - 1985 and 1988 - 1989 and 21 cases reported in Leningrad in 1988 - 1989. Immunodeficiency produced a significant effect on the severity of the cytomegaly. All cases included typical, often chronic sialodenitis with giant cell metamorphosis of the efferent ducts of the salivary gland; fibrosis of the duct stroma and lymphoid infiltrates in it. Other findings included generalized infection involving the lungs, liver, kidney, brain, pancreas and adrenals, myocardium and pancreas. Generalized cytomegalovirus infection observed in morphological studies was confirmed by detecting DNA of the virus with the use of the polymerase chain reaction. Other observations showed accidental transformation of the thymus of II or III degree. Figures 2; references 8: 5 Russian, 3 Western.

Antigenic Characteristics of Influenza A (H3N2) Viruses, Isolated in Kazakh SSR in 1987-1988

917C0122 Alma-Ata VESTNIK AKADEMII NAUK KAZAKHSKOY SSR in Russian Vol 10, Oct 90 pp 63-66

[Article by I. L. Kolyvanova, M. A. Yakhno, M. Kh. Sayatov and S. R. Bulgakova]

UDC 578.832.1:616-036.2:616-02

[Abstract] Specific features of the epidemic process during the 1987 - 1988 flu epidemic in the Kazakh SSR prompted a study of antigenic interconnections of influenza A (H3N2) viruses as the basic etiological agent of the epidemic. The study included examination of nasopharyngeal smears from children and adults hospitalized in Alma-Ata, with isolation of viruses on 10- to 11-day-old chick embryos. Comparative analysis in a hemagglutination inhibition reaction with standard polyclonal serums of the strain isolated in Alma-Ata represented a more or less homogeneous or antigenically similar group. Use of a series of monoclonal antibodies to actual drift variants of the flu virus showed significant differences within the group studied. Three isolates isolated from the same family on the same day showed significant differences in antigenic characteristics. Differences in the structure of these viruses were attributed to the individual immune status of the host organism, affecting the microheterogeneity of the antigenic composition of the hemagglutinin. Possibly the infectious agent either was originally a mixture of several antigenically different substrains or inter-strain recombinants may originate in the body of infected persons during joint circulation of the dominant and concomitant drift-variants. The antigenic analysis confirmed the recently revealed tendency toward an undeviating decrease of quantitative properties of earlier influenza pathogens in favor of the latest epidemically significant strains and showed the possibility of combined circulation of strains possessing different antigenic characteristics. References 10: 6 Russian, 4 Western.

Inactivation of AIDS Virus

917C0237A Moscow DOKLADY AKAKEMII NAUK SSSR in Russian Vol 314 No 3, Sep 90 (manuscript received 25 May 90) pp 739-741

[Article by K. Ya. Kondratyeva, academician, D. N. Nosik, T. A. Telegina, M. N. Korneyeva, N. V. Kuznetsova and P. P. Fedchenko, Institute of Biochemistry imeni A. N. Bakh, USSR Academy of Sciences, Moscow]

UDC 578.858

[Abstract] Trials were conducted on the inactivation of HIV-1 virus by 0.1 W visible magnesium radiation. HIV-1 samples irradiated for 20, 40 or 90 min were then used for infection of TM-4 and CEM cell cultures monitored for CPE and viability. Selection of MT-4 and CEM cells was based on their use as model systems for acute and chronic AIDS, respectively. The results showed that cells treated with virus irradiated for 40 or 90 min displayed near control levels of replication and viability (89.1 - 96.4 percent); irradiation for 20 min did not inactivate HIV-1. Virus inactivation with visible light of the magnesium spectrum affects only the external viral membranes, suggesting that this approach to virus inactivation might find use in the design of diagnostic tests and vaccines. Tables 1; references 4: 3 Russian, 1 Western.

Control of Choline Receptors in Molluscan Neurons by Vitamin E

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[Article by V. A. Dyatlov, Institute of Physiology imeni A. A. Bogomolets, Ukrainian SSR Academy of Sciences, Kiev]

UDC 577.352

[Abstract] In view of the antioxidant action of vitamin E and its significance in limiting lipid peroxidation of membrane lipids, an analysis was conducted on the possible role of vitamin E in cholinoreceptor topography in the edible snail. Electrophysiological studies on neurons isolated from brain ganglia of snails maintained for two months on either vitamin E deficient or E enriched diet involved assessment of membrane potentials in response to application of Ca^{++}, vitamin E, or acetylcholine. The results demonstrated that in both groups of snails, vitamin E led to activation of choline receptors and an increase in the number of receptors located distally to the axon. The control of distribution of the mobile receptors was evidently due to an increase in intracellular Ca^{++} and activation of Ca^{++}/calmodulin-dependent protein kinase. The smaller effect of exogenous calcium and the additive nature of calcium + vitamin E combination suggests that vitamin E influences intracellular calcium levels, membrane and cytoskeleton. Figures 3; references 9: 5 Russian, 4 Western.

Novel Type of Recombinant Protein Induction: Low Temperature Induction of Luciferase Gene Expression in Escherichia Coli

917C0237C Moscow DOKLADY AKAKEMII NAUK SSSR in Russian Vol 314 No 3, Sep 90 (manuscript received 21 Mar 90) pp 757-761

[Article by G. D. Kutuzova, Ye. A. Skrupkin, N. G. Belogurova, G. A. Skryabin, N. N. Ugarova and S. D. Varfolomeyev, Moscow State University imeni M. V. Lomonosov]

UDC 577.158.54

[Abstract] An interesting phenomenon of low-tempeature induction of recombinant luciferase gene induction has been observed in E. coli in which the firefly Photinus pyralis luciferase gene was incorporated into thermoinducible plasmid pME61. pME61 was constructed from plasmid pMM40, containing λP_R promoter and phage fd terminators, and plasmid pSV232AL-AΔ5'bearing the luciferase gene. Studies on the kinetics of luciferase expression in transformed E. coli showed a 120-fold increase in enzyme activity after 30 - 35 h at 21°C following induction for 2.5 h at 42°C, with the cell counts and plasmid numbers remaining constant. The level of luciferase activity was directly related to the duration of incubation at 42°C, with maximum activity obtained with 2.5 h at 42°C. Although the mechanisms underlying low-temperature induction remains enigmatic, biochemical studies indicate that depressed synthesis of cI repressor at 21°C may well have been a factor, while translation of luciferase mRNA proceeds unabated. At 21°C intracellular luciferase retained its activity for two weeks, whereas the half-life in cell lysates was ca. 3 h. Consequently, the high activity was due to ongoing transcription and translation as well as greater stability within the cellular milieu. If applicable to other systems, low-temperature inducton may well be a universal mechanism for increasing the yield of recombinant proteins. Figures 3; references 10: 3 Russian, 7 Western.

CNS Neurohumoral Regulatory Mechanisms in Experimental Influenza

917C0237D Moscow DOKLADY AKAKEMII NAUK SSSR in Russian Vol 314 No 3, Sep 90 (manuscript received 25 Jan 90) pp 764-767

[Article by B. A. Frolov, G. N. Smagin, V. K. Filippov, A. A. Nikiforov, A. A. Stadnikov, I. Yu. Kildivatov, R. Ya. Polyak and L. K. Chetverikova, Orenburg State Medical Institute; Institute of Experimental Medicine, USSR Academy of Medical Sciences, Leningrad]

UDC 616.921.5.001:612.43/.45

[Abstract] In view of the absence of an unambiguous relationship between antiviral resistance and the outcome of influenza, an analysis was conducted on potential pathogenetic mechanisms involving neuroendocrine and opioid systems in influenza. Accordingly, studies were performed on (CBA x C57Bl6)F_1 mice intranasally infected with either a 3.5 or 5.5 log EID_{50} dose of APR8/34/H1N1 influenza virus with monitoring of serum and hypothalamic levels of vasopressin and beta-endorphin, and serum ACTH and corticosterone dynamics. The results demonstrated that in lethal cases hypothalamic levels of vasopressin rose to statistically significant levels, particularly in the agonal stages (day 7), while serum levels were significantly depressed, indicating impaired transport across the blood-brain barrier. Determinations of beta-endorphin revealed marked

enhancment of synthesis in the lethal cases in comparison with mice subjected to nonlethal doses of influenza. Finally, endocrine monitoring revealed onset of adrenocortical insuffiency in mice with a lethal outcome. Comparison of the minimal changes seen in animals that survived and the pronounced imbalance in neuroendocrine and opioid systems in the lethal cases of murine influenza was interpreted to indicate the signal importance of such pathogenetic mechanisms in the progression and outcome of influenze. Figures 1; tables 1; references 15: 10 Russian, 5 Western.

L-DOPA and Dopamine Levels and Behavioral Patterns of Young Aequidens Pulcher Fish

917C0238A Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 314 No 5, Oct 90 (manuscript received 13 Mar 90) pp 1263-1267

[Article by I. V. Nechayev, B. P. Legkiy and Yu. A. Labas, Institite of Evolutionary Morphology and Ecology of animals imeni A. N. Severtsov, USSR Academy of Sciences, Moscow]

UDC 577.15/.17.577.95.591.329.597.5

[Abstract] An analysis was conducted on the levels of L-DOPA and dopamine in one-month-old Aequidens pulcher fish in relation to behavior, in view of the strong territorial instincts and aggressiveness of the adults. The results showed that the fry could be classified into two groups: animals with high and low levels of L-DOPA and dopamine, with the differences statistically significant. However, in both groups L-DOPA/dopamine ratios were constant and equivalent, and the groups did not differ in epinephrine and norepinephrine concentrations. Fry with high concentrations exhibited a much higher degree of searching behavior in 'open field' trials and also were intermediate in weight, with fish at the extremes of the weight spectrum falling into the low L-DOPA and dopamine group. The fry did not exhibit territoriality or aggressiveness as did the adults, which are characterized by much lower concentrations of L-DOPA and dopamine. This communication appears to be the first report on a correlation between behavior and catecholamine levels in vertebrate ontogeny. Figures 1; tables 2; references 8: 4 Russian, 4 Western.

Recombinant Vaccia Virus Bearing Hepatitis B $preS_2$-S Protein: Vaccination of Experimental Animals

917C0260A Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 314 No 2, Sep 90 (manuscript received 16 Jan 90) pp 488-491

[Article by A. S. Belyayev, I. P. Dmitriyev, G. M. Ignatyev, G. A. Mizenko, N .I. Putintseva, A. N. Sabirov, V. V. Samukov, L. N. Semenova, A. D. Ammosov, M. Yu. Rukavishnikov, I. N. Krasavina, P. Yu. Muratov, N. N. Mikryukov, L. R. Shevlyagina, A. P. Konstantinov and L. S. Sandakhchiyev, corresponding member, USSR Acad. Sci., All-Union Scientific Research Institute of Molecular Biology, Koltsovo, Novosibirsk Oblast]

UDC 575:616.912-085.371:616.36-002

[Abstract] Conventional techniques of genetic engineering were utilized for the construction of a recombinant vaccinia virus expressing the $preS_2$-S protein of hepatitis B virus [Cheng, KC, et al., J. Virol., 61: 1286, 1987]. The recombinant virus (rec7.5S_3S), constructed from the standard Soviet vaccinia LIVP strain, was tested for its vaccine potential in rabbits, BALB/c mice and Macaca mulatta monkeys. The vaccinated animals developed cellular immunity against HBs, $preS_2$ and vaccinia virus antigens. In addition, rabbits and mice developed antibodies against $preS_2$ protein, HBsAg and vaccinia antigens. Monkeys, however, failed to develop antibodies against HBsAg on intradermal vaccination while responding against the other antigenic components. The lack of an antibody response against HBsAg in monkeys reflected the genera observation that HBsAg is a poor immunogen in primates. Since recovery from hepatitis B has been shown to be predicated on cellular immunity, these findings indicate that rec7.5S_2S may have potential application as a live vaccine. Figures 1; tables 2; references 14: 4 Russian, 10 Western.

Cytochrome P-450 in Detoxication of Thioethynyl Esters of Monothiophosphoric Acids

917C0260B Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 314 No 2, Sep 90 (manuscript received 08 May 90) pp 501-504

[Article by L. A. Vikhreva, N. N. Godovikov, S. A. Nedelkina, T. A. Pupova, R. I. Sagalnik, corresponding member, USSR Acad. Sci., and M. I. Kabachnik,academician, Institutes of Heteroorganic Compounds imeni A. N. Nesmeyanov (Moscow) and of Cytology and Genetics, Siberian Department Novosibirsk), USSR Academy of Sciences]

UDC 577.1

[Abstract] Toxicity of several cholinesterase inhibitors has been shown to involve inactivation of hepatic cytochrome P-450, an important factor in detoxication. To further ascertain the effects of such agents on cytochrome P-450, incubation studies were performed with microsomal suspensions derived from rat livers and the following inhibitors: $(C_2H_5O)_2P(O)$-S-R, where R = C:::C - C_4H_9 (I), CH_2C:::C-H (II), CH_2C:::C_3H_7, and $C(CH_3)C$:::C - C_3H_7, where ::: represents a triple bond. The results demonstrated that in the presence of NADP-H only the first two agents promoted degradation of cytochrome P-450. With the first compund, O,O-diethyl-S-hexinylthiophosphate, a 23.2 percent loss of

cytochrome P-450 occurred, while with the second agent, O,O-diethyl-S-propargylthiophosphate, an 11.7 percent reduction was observed. Destruction of cytochrome P-450 was attributed to the transforamtion of the active compounds into alkylmercaptans and then to the active alkylthioketones via prototropic isomerization. In addition, even in the absence of exogenous NAD-H, incubation with O,O-diethyl-S-hexinylthiophosphate resulted in a 6.2 percent reduction in cytochrome P-450. Figures 2; tables 1; references 11: 4 Russian, 7 Western.

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